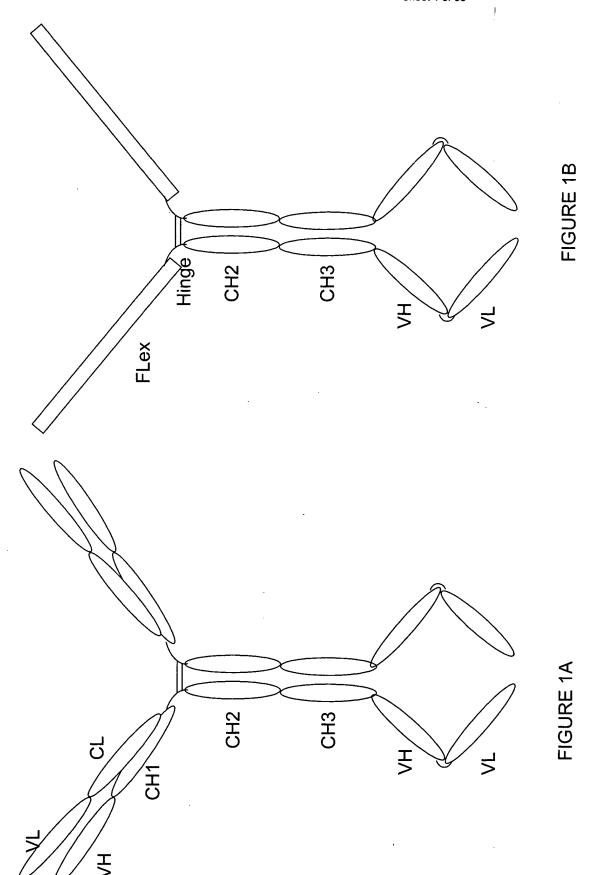
Docket No.: 549062000200

App No.: Not Yet Assigned Docket No.: 54
Inventor: Jing MA
Title: PREPARATION AND APPLICATION OF ANTI-TUMOR
BIFUNCTIONAL FUSION PROTEINS

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Title: PREPARATION AND APPLICATION OF ANTI-TUMOR BIFUNCTIONAL

FUSION PROTEINS

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Figure 2

	 →	SP																									
	M	Т	V	L	Α	Р	Α	W	S	P	Т	Т	Y	L	L	L	L	L	L	L	s	S	G	L	S		
0001	ATO	GAC	AGTO	CTC	GCC	CC	AGC	CTGC	GAG	CCC	AAC	'AAC	CTA	TCT	CCT	CTC	GCT	CTO	CTC	CTO	GAG	CTC	GGGA	CT)	CAGT	0075	

SP \leftarrow | \rightarrow FLex G T Q D C S F Q H S P I S S D F A V K I R E L S D 0076 GGGACCCAGGACTGCTCCTACAACACACACCCCATCTCCTCCGACTTCGCTGTCAAAATCCGTGAGCTGTCTGAC 0150

Y L L Q D Y P V T V A S N L Q D E E L C G G L W R 0151 TACCTGCTCAAGATTACCCAGTCACCGTGGCCTCCAACCTGCAGGACGAGGAGCTCTGGGGGGCCTCTGGCGG 0225

L V L A Q R W M E R L K T V A G S K M Q G L L E R 0226 CTGGTCCTGGCACAGCGCTGGATGGAGCGCTCAAGACTGTCGCTGGGTCCAAGATGCAAGACTTGCTGGAGCGC 0300

N I S R L L Q E T S E Q. L V A L K P W I T R Q N F 0376 AACATCTCCCGCCTCCTGCAGGAGCCTCCGAGCAGCTGGTGGGCGCTGAAGCCCTGGATCACTCGCCAGAACTTC 0450

S R C L E L Q C Q P D S S T L P P P W S P R P L E 0451 TCCCGGTGCCTGGAGTGCAGTGTCAGCCCGACCCCCATGGAGTCCCCGGCCCCTGGAG 0525

FLex←| A T A P T A P 0526 GCCACAGCCCCGACAGCCCCG

0546

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Figure 3

|-→SP M T V L A P A W S P T T Y L L L L L L S S G L S 0001 ATGACAGTGCTGGCGCCAGCCTGGAGCCCAACAACCTATCTCCTCCTGCTGCTGCTGCTGAGCTCGGGACTCAGT 0075

G T Q D C S F Q H S P I S S D F A V K I R E L S D 0076 GGGACCCAGGACTGCTCCAACACACGCCCCATCTCCTCCGACTTCGCTGTCAAAATCCGTGAGCTGTCTGAC 0150

Y L L Q D Y P V T V A S N L O D E E L C G G L W R 0151 TACCTGCTTCAAGATTACCCAGTCACCGTGGCCTCCAACCTGCAGGACGAGGAGGAGCTCTGCGGGGGGCCTCTGGCGG 0225

L V L A Q R W M E R L K T V A G S K M Q G L L E R 0226 CTGGTCCTGGCACGCGCTGGAGGGGCGCTCAAGACTGTCGCTGGGTCCAAGATGCAAGGCTTGCTGGAGCGC 0300

N I S R L L Q E T S E Q L V A L K P W I T R Q N F 0376 AACATCTCCCGCCTCCTGCAGGAGCCTCCGAGCAGCTGGTGGCGCTGAAGCCCTGGATCACTCGCCAGAACTTC 0450

S R C L E L Q C Q P D S S T L P P P W S P R P L E 0451 TCCCGGTGCCTGGAGCTGCAGTGTCAGCCCGACTCCTCAACCCTGCACCCCCATGGAGTCCCCGGCCCCTGGAG 0525

0526 GCCACAGCCCCGACAGCCCCGGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCAGCACCTGAA 0600

L L G G P S V F L F P P K P K D T L M I S R T P E 0601 CTCCTGGGGGGACCGTCATCTTCCTCTTCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAG 0675

V T C V V V D V S H E D P E V K F N W Y V D G V E 0676 GTCACATGCGTGGTGGACGTGACCCACGAAGACCCTGAGGTCAACTTCAACTGGTACGTGGACGGCGTGGAG 0750

V H N A K T K P R E E Q Y N S T Y R V V S V L T V 0751 GTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGGGTGGTCTGCGTCCTCACCGTC 0825

L H Q D W L N G K E Y K C K V S N K A L P A P I E 0826 CTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAG 0900

0901 AAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTG 0975

T K N Q V S L T C L V K G F Y P S D I A V E W E S 0976 ACCAAGAACCAGGTCAGCCTGGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGC 1050

N G Q P E N N Y K T T P P V L D S D G S F F L Y 1051 AATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTTCTTCCTCTACAGC 1125

K L T V D K S R W Q Q G N V F S C S V M H E A 1126 AAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCAC 1200

NHYTQKSLSLSPGK

1201 AACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCCGGTAAA

1242

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Figure 4

 ${\tt GGCGGTGGAGGCTCTGGTGGAGGCGGTTCAGGAGGCGGTGGATCT}$

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Lane 1: mSM5-1 heavy chain variable region Lane 2: mSM5-1 light chain variable region Lane 3: DL2000 DNA Marker

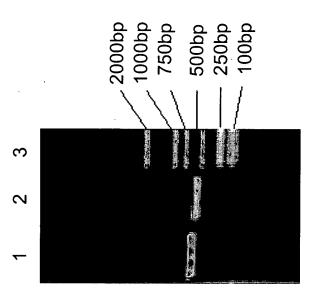


FIGURE 5

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Figure 6

SP←|→VH M E W S W I F L F L L S G T A G V H S E V
0001 ATCGCCGCCACCATGGAATGGAGTTGGATATTTCTCTTTCTCTTTCAGGAACTGCAGGTGTCCACTCTGAGGTC 0075 Q L Q Q S G P E L V K P G A S V K M S C K A S G Y 0076 CAGCTGCAGCAGTCTGGACCTGAGCTGGTAAAGCCTGGGGCTTCAGTGAAGATGTCCTGCAAGGCTTCTGGATAC 0150 T F T S Y V M H W V K Q K P G Q G L D W I G Y I V 0151 ACATTCACTAGCTATGTTATGCACTGGGTGAAGCAGAAGCCTGGGCAGGGCCTTGACTGGATTGGATATATTGTT 0225 P Y N D G T K Y N E K F K G K A T L T S D K S S S 0226 CCTTACAATGATGGCACTAAGTACAATGAGAAGTTCAAAGGCCACACTGACTTCAGACAAATCCTCCAGC 0300 T A Y M E L S R L T S E D S A V Y Y C V Y G S R Y 0301 ACAGCCTACATGGAGCTCAGCAGACTGACCTCTGAGGACTCTGCGGTCTATTATTGTGTCTACGGTAGTAGGTAC 0375 DWYLDVWGAGTTVTVSS 0376 GACTGGTATTTAGATGTCTGGGGCGCAGGGACCACGGTCACCGTCTCCTCA 0426

Figure 7

→SP MES 0001 ATCATCACCAGAACAGCTTACGAGCAGACCGCCAGACAGCTCACAGGGATCAAGCTTGCCGCCACCATGGAATCA 0075 $SP\leftarrow | \to V_L \\ Q \ T \ Q \ V \ F \ L \ S \ L \ L \ L \ W \ V \ S \ G \ T \ C \ G \ N \ I \ M \ M \ T \ Q \ S \ P \\ 0076 \ CAGACTCAGGTCTTCCTCTCCTGCTGCTCTTGGGTATCTGGGAACATTATGATGACACAGTCGCCA 0150 \\ \\$ S S L A V S A G E K V T M S C K S S Q S V L Y S S 0151 TCATCTCTGGCTGTCTGCAGGAGAAAGGTCACTATGAGCTGTAAGTCCAGTCAAAGTGTTTTATACAGTTCA 0225 N Q K N Y L A W Y Q Q K P G Q S P K L L I Y W A S 0226 AATCAGAAGAACTACTTGGCCTGGTACCAGCAGAAACCAGGGCAGTCTCCTAAACTGCTGATCTACTGGGCATCC 0300 T R E S G V P D R F T G S G S G T D F T L T I S S 0301 ACTAGGGAATCTGGTGTCCCTGATCGCTTCACAGGCAGTTGGTGTCTCGGACAGATTTTACTCTTACCATCAGCAGT 0375 V Q A E D L A V Y Y C H Q Y F S S Y T F G G G T K 0376 GTACAAGCTGAAGACCTGCAGTTTATTACTGTCATCAATATTTCTCCTCATACACGTTCGGAGGGGGGACCAAG 0450 0451 CTGGAAATAAAGCGG

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→SP SP← →VH M E W S W I F L F L L S G T A G V H S E V 0001 ATCGCCGCCACCATGGAATGGAGTTTGAATTTCTCTTTTCTCTGTCAGGAACTGCAGGTGTCCACTCTGAGGTC 0075
Q L Q Q S G P E L V K P G A S V K M S C K A S G Y 0076 CAGCTGCAGCAGTCTGGACCTGGACCTGGGGCTTCAGTGAAGATGTCCTGCAAGGCTTCTGGATAC 0150
T F T S Y V M H W V K Q K P G Q G L D W I G Y I V 0151 ACATTCACTAGCTATGTTATGCACTGGGTGAAGCAGAAGCCTGGGCAGGGCCTTGACTGGATATATTGTT 0225
PYNDCTKYNEKFKGKATLTSDKSSS 0226 CCTTACAATGACGACTAAGTACAATGAGAAGTCCAAAGCCAAAGCCACACCTGACTTCAGACAAATCCTCCAGC 0300
T A Y M E L S R L T S E D S A V Y Y C V Y G S R Y 0301 ACAGCCTACATGAGCTCAGCAGACTGAGCACTCTGAGGACTCTGCGGTCTATTATTGTGTCTACGGTAGTAGGTAC 0375
VH← →CH D W Y L D V W G A G T T V T V S S A S T K G P S V 0376 GACTGGTATTTAGATGTCTGGGGCGCAGGGACCACGGTCACCGTCTCCTCAGCTAGCACCAAGGGCCCATCGGTC 0450
F P L A P S S K S T S G G T A A L G C L V K D Y F 0451 TTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCTCAAGGACTACTTC 0525
PEPVTVSWNSGALTSGVHTFPAVLQ 0526 CCCGAACCGGTGACGTGTCTTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAG 0600
S S G L Y S L S S V V T V P S S S L G T Q T Y I C 0601 TCCTCAGGACTCTACTCCCTCAGCAGCTGGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGC 0675
N V N H K P S N T K V D K K V 0676 AACGTGAATCACAAGCCCAGCAACACCCAAGGTGGACAAGAAAGTTGGTGAGAGGCCAGCACAGGGAGGG
0751 TCTGCTGGAAGCAGGCTCAGCGCTCCTGCCTGGACGCATCCCGGCTATGCAGCCCCAGTCCAGGCCAGCCA
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E P K S C D
E P K S C D 1051 TCAGCTCGGACACCTTCTCCCCCAGATTCCAGTAACTCCCAATCTTCTCTCGCAGAGCCCAAATCTTGTGA 1125 K T H T C P P C P
E P K S C D 1051 TCAGCTCGGACACCTTCTCTCCCCAGATTCCAGTAACTCCCAATCTTCTCTCGCAGAGCCCAAATCTTGTGA 1125 K T H T C P P C P 1126 CAAAACTCACACATGCCCACCGTGCCCAGGCCCAGGCCTCGCCCTCCAGCTCAAGGCGGGACAGGTG 1200 A P 1201 CCCTAGAGTAGCCTGCATCCAGGGACAGGCCCCAGCCGGGTGCTGACACGTCCACCTCCATCTCTTCCTCAGCAC 1275 E L L G G P S V F L F P P K P K D T L M I S R T P
E P K S C D 1051 TCAGCTCGGACACCTTCTCCCCAGATTCCAGTAACTCCCAATCTTCTCTCGCAGAGCCCAAATCTTGTGA 1125 K T H T C P P C P 1126 CAAAACTCACACATGCCCACCGTGCCCAGGTAAGCCAGGCCCAGGCCTCCAGCTCAAGGCGGGACAGGTG 1200 A P 1201 CCCTAGAGTAGCCTGCATCCAGGGACAGGCCCCAGCCGGGTGCTGACACGTCCACCTCCATCTCTCTC
E P K S C D 1051 TCAGCTCGGACACCTTCTCTCCCCAGATTCCAGTAACTCCCAATCTTCTCTCGCAGAGCCCAAATCTTGTGA 1125 K T H T C P P C P 1126 CAAAACTCACACATGCCCACCGTGCCCAGGTAAGCCAGGCCTCGCCCTCCAGCTCAAGGCGGGACAGGTG 1200 A P 1201 CCCTAGAGTAGCCTGCATCCAGGGACAGGCCCCAGCCGGGTGCTGACACGTCCACCTCCATCTCTCCTCAGCAC 1275 E L L G G P S V F L F P P K P K D T L M I S R T P 1276 CTGAACTCCTGGGGGGGACCGTCAGTCTTCCTCTCCCCCCAAAACCCCAAGGACACCCTCCATGATCTCCCGGACCC 1350
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E P K S C D 1051 TCAGCTCGGACACCTTCTCTCCCCAGATTCCAGTAACTCCCAATCTTCTCTCTGCAGAGCCCAAATCTTGTGA 1125 K T H T C P P C P 1126 CAAAACTCACACATGCCCACCGTGCCCAGGTAAGCCAGGCCCAGGCCTCGCCCTCCAGCTCAAGGCGGGACAGGTG 1200 L201 CCCTAGAGTAGCCTGCATCCAGGGACAGGCCCCAGCCGGGTGCTGACACGTCCACCTCCATCTCTCTC
E P K S C D 1051 TCAGCTCGGACACCTTCTCTCCCCAGATTCCAGTAACTCCCAATCTTCTCTCTGCAGAGCCCAAATCTTGTGA 1125 K T H T C P P C P 1126 CAAAACTCACACATGCCCACCGTGCCCAGGTAAGCCAGGCCCAGGCCTCGCCCTCCAGCTCAAGGCGGGACAGGTG 1200 A P 1201 CCCTAGAGTAGCCTGCATCCAGGGACAGGCCCCAGGCCGGGTGCTGACACGTCCACCTCCATCTCTCCTCAGCAC 1275 E L L G G P S V F L F P P K P K D T L M I S R T P 1276 CTGAACTCCTGGGGGGACCGTCAGTCTTCCTCTCTCCCCCCAAAACCCCAAGGACACCCTCATGATCTCCCGGACCC 1350 E V T C V V V D V S H E P E V K F N W Y V D D G V 1351 CTGAGGTCACATGCGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGC 1425 E V H N A K T K P R E E Q Y N S T Y R V V S V L T 1426 TGGAGGTGCATAATGCCAAGACAAAGCCGGGGAGGAGGAGACACGTACCGGGTGGTCTCCTCTCTCT
E P K S C D 1051 TCAGCTCGGACACCTTCTCTCCCCAGATTCCAGTAACTCCCAATCTTCTCTCTGCAGAGCCCAAATCTTGTGA 1125 K T H T C P P C P 1126 CAAAACTCACACATGCCCACCGTGCCCAGGTAAGCCAGGCCCAGGCCTCGCCCTCCAGCTCAAGGCGGGACAGGTG 1200 A P 1201 CCCTAGAGTAGCCTGCATCCAGGGACAGGCCCCAGGCCGGGTGCTGACACGTCCACCTCCATCTCTTCCTCAGCAC 1275 E L L G G P S V F L F P P K P K D T L M I S R T P 1276 CTGAACTCCTGGGGGGACCGTCAGTCTTCCTCTCTCCCCCCAAAACCCCAAGGACACCCTCATGATCTCCCGGACCC 1350 E V T C V V V D V S H E P E V K F N W Y V D D G V 1351 CTGAGGTCACATGCGTGGTGGACCGTGAGCCACGAAGACCCTGAGGTCAACTGTACCTGGACGGCG 1425 E V H N A K T K P R E E Q Y N S T Y R V V S V L T 1426 TGGAGGTGCATAATGCCAAGACCAAAGCCGGGGAGGAGACACAGACACGTACCGGGTGGTCTCCTCA 1500 V L H Q D W L N G K E Y K C K V S N K A L P A P I 1501 CCGTCCTGCACCAGGACTGCTGAATGCCAAAGCCAAGGCACGTACCAGACACAAAGCCCTCCAGCCCCCA 1575 E K T I S K A K 1576 TCGAGGAAAAACCATCTCCAAAGCCAAAGCCGAAGGCCCGTGGGGTGCGAGGGCCACATGGACAGAGGCCGGCC
E P K S C D 1051 TCAGCTCGGACACCTTCTCCCCAGATTCCAGTAACTCCCAATCTTCTCTCGCAGAGCCCAAATCTTGTGA 1125 K T H T C P P C P 1126 CAAAACTCACACATGCCCACCGTGCCCAGGTAAGCCAGGCCCAGGCCTCCAGCTCCAGGCGGGACAGGTG 1200 L201 CCCTAGAGTAGCCTGCATCCAGGGACAGGCCCCAGGCCGGGTGCTGACACGTCCACCTCCATCTCTTCGTCAGCAC 1275 E L L G G P S V F L F P P K P K D T L M I S R T P 1276 CTGAACTCCTGGGGGACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCCATGATCTCCCGGACCC 1350 E V T C V V D V S H E P E V K F N W Y V D D G V 1351 CTGAGGTCACATGCTGGTGGTGGACCGTGAGCCCAGAAGACCCTGAGGTCAACTTGAACTGGTACGTGGACGGC 1425 E V H N A K T K P R E E Q Y N S T Y R V V S V L T 1426 TGGAGGTCATAATGCCAAGACAAAGCCGCGGGAGGACCACTACAGCACCGTCCCCCCA 1500 V L H Q D W L N G K E Y K C K V S N K A L P A P I 1501 CCGTCCTGCACCAGGACTGGCTGAATGGCAAGGTACAAGTGCAACGTCTCCAACAAAGCCCTCCAGCCCCCA 1575 E K T I S K A K 1576 TCGAGAAAACCATCTCCAAAGCCAAAGGCGGGGACCCGTGGGGTGCGAGGGCCACATGGACAGAGCCCTCCAGCCCCCA 1650 C Q P R E P Q V Y T 1651 CCACCCTCTGCCCTGAGAGTGACCGCTGTACCAACCTCTTTCCTTCC
E P K S C D 1051 TCAGCTCGGACACCTTCTCCCCCAGATTCCAGTAACTCCCAATCTTCTCTCGCAGAGCCCAAACCTTGTGA 1125 K T H T C P P C P 1126 CAAAACTCACACATGCCCACCGTGCCCAGGTAAGCCAGGCCCAGGCCTCGCCCTCCAGGCCGAAGGTG 1200 A P 1201 CCCTAGAGTAGCCTGCATCCAGGGACAGGCCCAGGCCCAGGCTGACCGCCCCCACCTCCATCTCTCCTCAGCAC 1275 E L L G G P S V F L F P P K P K D T L M I S R T P 1276 CTGAACTCCTGGGGGGACCGTCGTCTCTCTCTCTCCCCCCAAAACCCCAAGGACACCCTCCATGTCTCCCCGGACCC 1350 E V T C V V V D V S H E P E V K F N W Y V D D G V 1351 CTGAGGTCACATGCGTGGTGGACCGTGAGCCACGAGAGCCCCTGAGGTCAACTTCAACTGGTACGTGGACGGC 1425 E V H N A K T K P R E E Q Y N S T Y R V V S V L T 1426 TGGAGGTGCATAATGCCAAGACCAAAAGCCGGGAGGACACGTACACAGCACGTCCCCGGTGCTCTCA 1500 V L H Q D W L N G K E Y K C K V S N K A L P A P I 1501 CCGTCCTGCACCAGGACTAGCCTGAATGGCAAGGACCACAGGTCCAACAAAGCCCTCCCAGCCCCCA 1575 E K T I S K A K 1576 TCGAGAAAACCATCTCCAAAGCCAAAGGTGGAACGAGGGCCACATGGACAGAGGCCGGCTCGGC 1650 G Q P R E P Q V Y T 1651 CCACCCTCTGCCCTGAGAGTGACCGCTGTACCAACCACCTCTGTCCTACAGGGCCACCCCGAGAACCACAGGTGTACA 1725 L P P S R D E L T K N Q V S L T C L V K G F Y P S 1726 CCCTGCCCCCCATCCCGGGATGACCAAGACCCAAGAACCCTCTGTCCTACAAGGCCTGGCTGG

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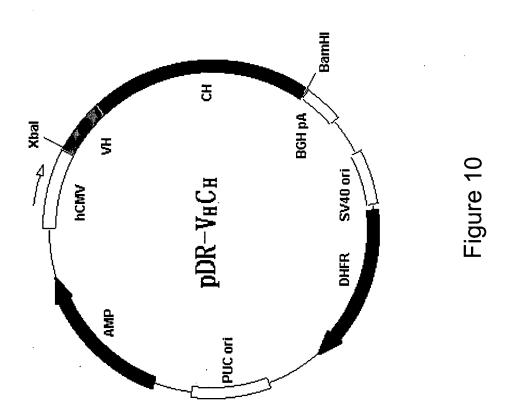
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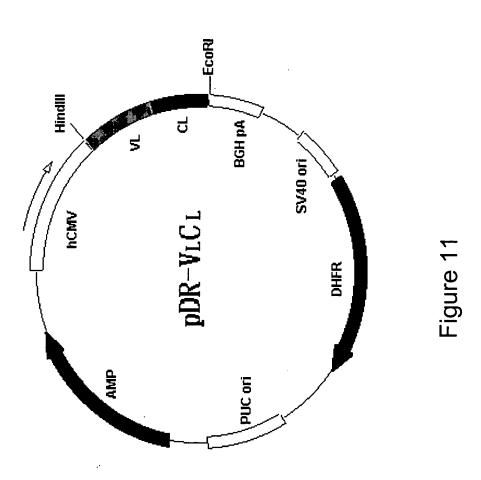
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→SP M D F Q V																											
O001 GAGCATTACCGGCCATACTCATCACCATCCCAGGATATCTCTAGAAAGCTTGCCGCCACCATGGATTTTCAAGTG 0075 SP← →V _L Q I F S F L L I S A S V I M S R G N I M M T Q S P O006 CAGATTTTCAGCTTCCTGCTAATCAGTGCTTCAGTCATAATGTCCAGAGGAAACATCATGATGACTCAGAGCCCA 0150 S S L S A S V G D R V T I T C K S S Q S V L Y S S O151 TCCAGCTTGAGCGCATCAGTAGGCGACCGCGTAACGATCACTTGCAAATCCTCTCAGTCAG																						 → :	SP				
SP← →V _L Q I F S F L L I S A S V I M S R G N I M M T Q S P 0076 CAGATTTTCAGCTTCCTGCTAATCAGTGCTTCAGTCATAATGTCCAGAGGAAACATCATGATGACTCAGAGGCCCA 0150 S S L S A S V G D R V T I T C K S S Q S V L Y S S 0151 TCCAGCTTGAGCGCATCAGTAGGCGACCGCGTAACGATCACTTGCAAATCCTCTCAGTCAG																											
Q I F S F L L I S A S V I M S R G N I M M T Q S P 0076 CAGATTTCAGCTTCCTGCTAATCAGTGCTTCAGTCATAATGTCCAGAGGAAACATCATGACTGAC	0001	GA	GCA'	TTA	CCG	GCC	АТА	CTC	АТС	ACC	ATC	CCA	GGA	TAT	CTC	TAG	AAA	GCT	TGC	CGC	CAC	CAT	'GGA	TTT	TCA	AGTG	0075
O076 CAGATTTCAGCTTCCTGCTAATCAGTGCTTCAGTCATAATGTCCAGAGGAAACATCATGACTGAC																	5	₽←	→ V	L							
S S L S A S V G D R V T I T C K S S Q S V L Y S S 0151 TCCAGCTTGAGCGCATCAGTAGGCGACCGCGTAACGATCACTTGCAAATCCTCTCAGTCAG		Q	I	F	s	F	L	L	1	s	A	S	v	I	M	s	R	G	N	I	М	М	Т	0	s	P	
0151 TCCAGCTTGAGCGCATCAGTAGGCGACCGCGTAACGATCACTTGCAAATCCTCTCAGTCAG	0076	CA	GAT"	TTT(CAG	CTT	CCT	GCT	AAT	CAG	TGC	TTC	AGT	CAT.	AAT	GTC	CAG	AGG	AAA	CAT	CAT	'GAT	GAC	TCA	GAG	CCCA	0150
0151 TCCAGCTTGAGCGCATCAGTAGGCGACCGCGTAACGATCACTTGCAAATCCTCTCAGTCAG		s	s	τ.	s	А	s	v	G	מ	R	v	т	т	т	~	к	S	s	0	S	v	т.	v	S	q	
0226 AACCAGAAGAACTACCTGGCCGGATATCAGCAGACTCCCGGCAAAGCCCCAAAGTTGCTGATTTATTGGGCCTCC 0300 T R E S G V P S R F S G S G T D Y T F T I S S 0301 ACGCGCGAGTCTGGCCTGCCATCACGCTTTAGCGGCAGCGGGTCCGGTACAGATTACACGTTTACCATTAGCAGT 0375 L Q P E D I A T Y Y C H Q Y F S S Y T F G Q G T K	0151																										0225
0226 AACCAGAAGAACTACCTGGCCGGATATCAGCAGACTCCCGGCAAAGCCCCAAAGTTGCTGATTTATTGGGCCTCC 0300 T R E S G V P S R F S G S G T D Y T F T I S S 0301 ACGCGCGAGTCTGGCCTGCCATCACGCTTTAGCGGCAGCGGGTCCGGTACAGATTACACGTTTACCATTAGCAGT 0375 L Q P E D I A T Y Y C H Q Y F S S Y T F G Q G T K			^	7,		.,			*.*		_	_	_	_	_	.,									_	_	
T R E S G V P S R F S G S G S G T D Y T F T I S S 0301 ACGCGCGAGTCTGGCGTCACGCTTTAGCGGCAGCGGGTCCGGTACAGATTACACGTTTACCATTAGCAGT 0375 L Q P E D I A T Y Y C H Q Y F S S Y T F G Q G T K	0226																										0300
0301 ACGCGCGAGTCTGGCGTGCCATCACGCTTTAGCGGCAGCGGGTCCGGTACAGATTACACGTTTACCATTAGCAGT 0375 L Q P E D I A T Y Y Y C H Q Y F S S Y T F G Q G T K																											
LQPEDIATYYCHQYFSSYTFGQGTK	0301																										0275
	0301	7100	5000	COM		100		-		ACG		IAG	-	CAG	CGG	GIC	CGG	IAC	AUA	110	CAC	GII	IAC	CAI	IAG	CAGI	0373
- U.S. 76 - CTU-CAG-CCTG-AC-GCAG-AC-AC-CCTACTTACTTG-CACTTACTTACTTG-TTACTTG-TTACTCTTTTTTTCCCCACG-GAG-GAAAAA AAAA	0276																										
U CONTROL CONT	03/6	CTC	JCA(الالال	ľGA	GGA	JAT	AGC	CAC	CTA	CTA	CTG	rca	CCA	GTA	CTT	TAG	FFC	CTA	CAC	1.1.1.	TGG	ÇCA	GGG	AAC	TAAA	0450
V _L ←-						- •																					
L Q I T R. 0451 CTGCAGATTACTCGA 0465	0451	_	-	_	_																						0465

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Q L V Q S G G G V V Q P G R S L R L S C K A S G Y 0076 CAGCTGGTGCAGTCTGGCGAGTGGTCCAGCCCGGCCGCAGCCTGAGGCTGTCCTGCAAGGCATCTGGCTAC 0150
T F T S Y V M H W V R Q A P G K G L E W I G Y I V 0151 ACCTTCACCAGCTACGTGACATGGGTGCGCCAAGCCCCCGGAAAGGGCCTCGAATGGATTGGCTACATTGTG 0225
PYNDGTKYNEKFKGRFTISSDKSKS 0226 CCTTATAATGACGGTACTAAGTACAATGAAAAGTTCAAGGGCAGTTACAATATCAAGTGACAAGAGCAAGTCA 0300
T A F L Q M D S L R P E D T A V Y Y C A R G S R Y 0301 ACCGCATTCCTCCAAATGGACAGCTTGCGTCCAGAGGACACCGCCGTATACTATTGTGTGCGCGGCAGCCGTTAC 0375
VH← →CH D W Y L D Y W G Q G T P V T V S S A S T K G P S V 0376 GACTGGTACTTGGACTACTGGGGCCAAGGCACTCCAGTCACCGTCTCCTCTGCTAGCACCAAGGGCCCATCGGTC 0450
F P L A P S S K S T S G G T A A L G C L V K D Y F 0451 TTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGGTCAAGGACTACTTC 0525
P E P V T V S W N S G A L T S G V H T F P A V L Q 0526 CCCGAACCGGTGACGGTGTCTTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAG 0600
S S G L Y S L S S V V T V P S S S L G T Q T Y I C 0601 TCCTCAGGACTTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGC 0675
N V N H K P S N T K V D K K V 0676 AACGTGAATCACAAGCCCAACACCAAGGTGGACAAGAAAGTT <u>GGTGAGAGGCCAGCACAGGGAGGGAGGGTG</u> 0750
0751 TCTGCTGGAAGCAGGCTCAGCGCTCCTGCCTGGACGCATCCCGGCTATGCAGCCCCAGTCCAGGGCAGCAAGGCA 0825
0826 GGCCCCGTCTGCCTCTTCACCCGGAGCCTCTGCCCGCCCCACTGATGCTCAGGGAGAGGGTCTTCTGGCTTTTTC 0900
0901 CCAGGCTCTGGGCAGGCACAGGCTAGGTGCCCCTAACCGAGGCCCTGCACACAAAGGGGCAGGTGCTGGGCTCAG 0975,
0976 ACCTGCCAAGAGCCATATCCGGGAGGACCCTGCCCCTGACCTAAGCCCACCCCAAAGGCCAAACTCTCCACTCCC 1050
E P K S C D 1051 TCAGCTCGGÁCACCTTCTCCCCAGATTCCAGTAACTCCCAATCTTCTCTGCAGAGCCCAAATCTTGTGA 1125
K T H T C P P C P 1126 CAAAACTCACACATGCCCACGGTGCCCAGGTCAAGGCCAGGTGAAGGCGGACAGGTG 1200
A P 1201 CCCTAGAGTAGCCTGCATCCAGGGACAGGCCCCAGCCGGGTGCTGACACGTCCACCTCCATCTCTCCTCAGCAC 1275
E L L G G P S V F L F P P K P K D T L M I S R T P 1276 CTGAACTCCTGGGGGGACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCC 1350
E V T C V V V D V S H E P E V K F N W Y V D D G V 1351 CTGAGGTCACTGGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAACTGGTACGTGGACGGCG 1425
E V H N A K T K P R E E Q Y N S T Y R V V S V L T 1426 TGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGGGTGGTCTGCGTCCTCA 1500
V L H Q D W L N G K E Y K C K V S N K A L P A P I 1501 CCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCA 1575
E K T I S K A K 1576 TCGAGAAAACCATCTCCAAAGCCAAAGGTGGGACCCGTGGGGTGCGAGGGCCACATGGACAGAGGCCGGCTCGGC 1650
G Q P R E P Q V Y T 1651 CCACCCTCTGCCCTGAGAGTGACCGCTGTACCAACCTCTGTCCTACAGGGCAGCCCCGAGAACCACAGGTGTACA 1725
L P P S R D E L T K N Q V S L T C L V K G F Y P S 1726 CCCTGCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCTGGCTGACAAGGCTTCTATCCCA 1800
D I A V E W E S N G Q P E N N Y K T T P P V L D S 1801 GCGACATCGCCGTGGAGGGGAGCAATGGGCAGCCGGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACT 1875
D G S F F L Y S K L T V D K S R W Q Q G N V F S C 1876 CCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCAT 1950
S V M H E A L H N H Y T Q K S L S L S P G K STOP 1951 GCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCCGGTAAATGA 2021

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Figure 15

|→SP

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M D F Q V 0001 GAGCATTACCGGCCATACTCATCACCATCCCAGGATATCTCTAGAAAGCTTGCCGCCACCATGGATTTTCAAGTG 0075

 $SP \leftarrow | \rightarrow V_L$

Q I F S F L L I S A S V I M S R G N I M M T Q S P 0076 CAGATTTTCAGCTTCCTGATCAGTGCTTCAGTGCTCAGAGGGAAACATCATGATGACTCAGAGGCCCA 0150

N Q K N Y L A W Y Q Q T P G K A P K L L I Y W A S 0226 AACCAGAAGAACTACCTGGCCGGATATCAGCAGACTCCCGGCAAAGCCCCAAAGTTGCTGATTTATTGGGCCTCC 0300

T R E S G V P S R F S G S G S G T D Y T F T I S S 0301 ACGCGCGAGTCTGGCGTGCCATCACGCTTTAGCGGCAGCCGGTACAGATTACACGTTTACCATTAGCAGT 0375

L Q P E D I A T Y Y C H Q Y F S S Y T F G Q G T K 0376 CTGCAGCCTGAGGACTAGCCACCTACTACTGCTCACCAGTACTTTTGGTCCTACACTTTTGGCCAGGGACTAAA 0450

 $V_L \leftarrow | \rightarrow C_L$ L Q I T R T V A A P S V F I F P P S D E Q L K S G 0451 CTGCAGATTACTCGAACTGTGGCTGCACCATCTGTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGA 0525

T A S V V C L L N N F Y P R E A K V Q W K V D N A 0526 ACTGCCTCTGTTGTGCCTGAATAACTTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTGGATAACGCC 0600

L Q S G N S Q E S V T E Q D S K D S T Y S L S S T 0601 CTCCAATCGGGTAACTCCCAGGAGGTGTCACAGAGCAGGACAGGACAGCACCTACAGCCTCAGCAGCACC 0675

L T L S K A D Y E K H K V \cdot Y A C E V T H Q G L S S 0676 CTGACGCTGAGCAAAGCTGCGAAAGCACAAAGTCTACGCCTGCGAAGTCACCCATCAGGGCCTGAGCTCG 0750

P V T K S F N R G E C Stop

0786

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Figure 16A

	¦→SP M D W V W T L L F L L S V T A G V H S Q V	
0001	AGAGCCGCCACCATGGATTGGGTGTGGACCTTGCTATTCCTGTTGTCAGTAACTGCAGGTGTCCACTCCCAGGTG Q L V Q S G G G V V Q P G R S L R L S C K A S G Y	0075
0076	${\tt CAGCTGGTGCAGTCTGGCGGTGGAGTCCCAGCCCGGCCGCAGCCTGAGGCTGTCCTGCAAGGCATCTGGCTAC}$	0150
0151	T F T S Y V M H W V R Q A P G K G L E W I G Y I V ACCTTCACCAGCTACGTGATGACATGGGTGCGCCAAGCCCCCGGAAAGGGCCTCGAATGGATTGGCTACATTGTG	0225
0226	P Y N D G T K Y N E K F K G R F T I S S D K S K S CCTTATAATGACGGTACTAAGTACAATGAAAAGTTCAAGGGCAGATTTACAATATCAAGTGACAAGAGCAAGTCA	0300
0301	T A F L Q M D S L R P E D T A V Y Y C A R G S R Y ACCGCATTCCTCCAAATGGACAGCTTGCGTCCAGAGGACACCGCCGTATACTATTGTGTGCGCGGCAGCCGTTAC	0375
0376	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	0450
0451	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	0525
0526	P E P V T V S W N S G A L T S G V H T F P A V L Q CCCGAACCGGTGACGGTGTCTTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAG	0600
0601	S S G L Y S L S S V V T V P S S S L G T Q T Y I C TCCTCAGGACTTCACTCCCTCAGCAGCGTGGTGACCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGC	0675
0676	N V N H K P S N T K V D K K V AACGTGAATCACAAGCCCAGCAACACCAAGGTGGACAAGAAAGTTGGTGAGAGGCCAGCACAGGAGGGGGGGG	0750
	TCTGCTGGAAGCAGGCTCAGCGCTCCTGCCTGGACGCATCCCGGCTATGCAGCCCCAGTCCAGGGCAGCAAGGCA	
0826	GGCCCCGTCTGCCTCTTCACCCGGAGCCTCTGCCCGCCCCACTCATGCTCAGGGAGAGGGTCTTCTGGCTTTTTC	0900
0901	CCAGGCTCTGGGCAGGCACAGGCTAGGTGCCCCTAACCCAGGCCCTGCACACAAAGGGGCAGGTGCTGGGCTCAG	0975
0976	${\tt ACCTGCCAAGAGCCATATCCGGGAGGACCCTGCCCCTGACCTAAGCCCAAAGGCCAAACTCTCCACTCCCCTGACCTAAGCCCAAAGGCCAAACTCTCCACTCCCCCCAAAGGCCAAAGGCCAAACTCTCCACTCCCCCAAAGGCCAAAGGCCAAACTCTCCACTCCCCCCAAAGGCCAAAGGCCAAACTCTCCACTCCCCCAAAGGCCAAAGGCCAAACTCTCCACTCCCCCCAAAGGCCAAAGGCCAAACTCTCCACTCCCCCCAAAGGCCAAAAGGCCAAAACTCTCCACTCCCCCCAAAGGCCAAAACTCTCCACTCCCCCCAAAGGCCAAAACTCTCCACTCCCCCCAAAGGCCAAAACTCTCCACTCCCCCCAAAGGCCAAAACTCTCCACTCCCCCCAAAGGCCAAAACTCTCCACTCCCCCCCAAAGGCCAAAACTCTCCACTCCCCCCAAAGGCCAAAACTCTCCACTCCCCCCAAAGGCCAAAACTCTCCACTCCCCCCAAAGGCCAAAACTCTCCACTCCCCCCAAAGGCCAAAACTCTCCACTCCCCCCAAAGGCCAAAACTCTCCACTCCCCCCAAAAGGCCAAAACTCTCCACTCCCCCCAAAAGGCCAAAACTCTCCACTCCCCCCAAAAGGCCAAAACTCTCCACTCCCCCCAAAAGGCCAAAACTCTCCACTCCCCCCAAAAGGCCAAAACTCTCCACTCCCCCAAAAGGCCAAAACTCTCCACTCCCCCAAAAGGCCAAAACTCTCCACTCCCCCAAAAGGCCAAAACTCTCCACTCCCCCAAAAGGCCAAAACTCTCCACTCCCCAAAAGGCCAAAACTCTCCACTCCCCCCAAAAGGCCAAAACTCTCCACTCCCCCAAAAGGCCAAAACTCTCCACTCCCCCCAAAAGGCCAAAACTCTCCACTCCCCCCAAAAGGCCAAAACTCTCCACTCCCCCCAAAAGGCCAAAACTCTCCACTCCCCCCAAAAGGCCAAAACTCTCCACTCCCCCCAAAAGGCCAAAACTCCCCAAAAGGCCAAAACTCCCCAAAAGGCCAAAACTCCCCCAAAAGGCCAAAACTCCCCAAAAGGCCAAAACTCCCCAAAAGGCCAAAACTCCCCAAAAGGCCAAAACTCCCAAAAGGCCAAAACTCCAAAAGGCCAAAACTCCCCAAAAGGCCAAAACTCCCAAAAAGGCCAAAACTCCCAAAAGCCCAAAACTCAAAAAAAA$	1050
1051	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	1125
1126	K T H T C P P C P CAAAACTCACACATGCCCACGTGCCCAGGTAAGCCAGGCCCAGGCCTCCAGCTCAAGGCGGGACAGGTG	1200
1201	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	1275
1276	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	1350
1351	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	1425
1426	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	1500
1501	V L H Q D W L N G K E Y K C K V S N K A L P A P I CCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCA	1575
1576	E K T I S K A K TCGAGAAAACCATCTCCAAAGCCAAAGGTGGGACCCGTGGGGTGCGAGGGGCCACATGGACAGAGGCCGGCTCGGC	L 6 50
1651	G Q P R E P Q V Y T CEACCCTCTGCCCTGAGAGCCCCGAGAACCACAGGTGTACA	1725
1726	L P P S R D E L T K N Q V S L T C L V K G F Y P S CCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACÇAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCA	.800
1801	D I A V E W E S N G Q P E N N Y K T T P P V L D S GCGACATCGCCTGGAGGGAGGAACAACTACAAGACCACGCCTCCCGTGCTGGACT 1 $$.875
1876	D G S F F L Y S K L T V D K S R W Q Q G N V F S C CCGACGGCTCCTTCTCTCACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCAT 1	.950
1951	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	025

C S F Q H S P I S S D F A V K I R E L S D Y L L Q 2026 ACTGCTCCTCCAACACACACCCCATCTCCTCCGACTTCGCTGTCAAAATCCGTGAGTGTCTGACTACCTGCTTC 2100 D Y P V T V A S N L Q D E E L C G G L W R L V L A 2101 AAGATTACCCAGTCACCGTGGCCTCCAACCTGCAGGACGAGGAGGTCTGCGGGGGGCCTCTGGCGGGCTGGTCCTGG 2175 Q R W M E R L K T V A G S K M Q G L L E R V N T E 2176 CACAGCGCTGGATGGAGCGGCTCAAGACTGTCGCTGGGTCCAAGATGCAAGGCTTGCTGGAGCGCGTGAACACGG 2250 L L Q E T S E Q L V A L K P W I T R Q N F S R C L 2326 GCCTCCTGCAGGAGCCTCCGAGCAGCTCGCTGGCC 2400 E L Q C Q P D S S T L P P P W S P R P L E A T A 2401 TGGAGCTGCAGTGTCAGCCCGACTCCTCAACCCTGCCACCCCATGGAGTCCCCGGCCCCTGGAGGCCACAGCCC 2475 T A P STOP 2476 CGACAGCCCCGTGA

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FUSION PROTEINS

Figure 16B

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Figure 17A

→SP
M D W V W T L L F L L S V T A G V H S Q V 0001 AGAGCCGCCACCATGGATTGGGTGGACCTTGCTATTCCTGTTGTCAGTAACTGCAGGTGTCCACTCCCAGGTG 0075
Q L V Q S G G G V V Q P G R S L R L S C K A S G Y 0076 CAGCTGGTGCAGTCTGGCGGTGGGGTGGTCCAGCCCGGCCGCAGCCTGAGGCTGTCCTGCAAGGCATCTGGCTAC 0150
T F T S Y V M H W V R Q A P G K G L E W I G Y I V 0151 ACCTTCACCAGCTACGTGATGACATGGGTGCGCCAAGCCCCCGGAAAGGGCCTCGAATGGATTGGCTACATTGTG 0225
PYNDGTKYNEKFKGRFTISSDKSKS 0226 CCTTATAATGACGGTACTAAGTACAATGAAAAGTTCAAGGGCAGATTTACAATATCAAGTGACAAGAGCAAGTCA 0300
T A F L Q M D S L R P E D T A V Y Y C A R G S R Y 0301 ACCGCATTCCTCCAAATGGACAGCTTGCGTCCAGAGGACACCGCCGTATACTATTGTGTGCGCGGCAGCCGTTAC 0375
VH← →CH DWYLDYWGQGTPVTVSSASTKGPSV 0376 GACTGGTACTTGGACTACTGGGGCCCAAGGCACTCCAGTCACCGTCTCCTCTGCTAGCACCAAGGGCCCATCGGTC 0450
F P L A P S S K S T S G G T A A L G C L V K D Y F 0451 TTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGGTCAAGGACTACTTC 0525
PEPVTVSWNSGALTSGVHTFPAVLQ 0526 CCCGAACCGGTGACGGTGTCTTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAG 0600
S S G L Y S L S S V V T V P S S S L G T Q T Y I C 0601 TCCTCAGGACTTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGC 0675
N V N H K P S N T K V D K K V 0676 AACGTGAATCACAAGCCCAGCAACACCAAGGTGGACAAGAAAGTTG <u>GTGAGAGGCCAGCACAGGGAGGGAGGGTG</u> 0750
0751 TCTGCTGGAAGCAGGCTCAGCGCTCCTGCCTGGACGCATCCCGGCTATGCAGCCCCAGTCCAGGGCAGCAAGGCA 0825
0826 GGCCCGTCTGCCTCTTCACCCGGAGCCTCTGCCCGCCCCACTCATGCTCAGGGAGAGGGTCTTCTGGCTFTTTC 0900
0901 CCAGGCTCTGGGCAGGCACAGGCTAGGTGCCCCTAACCCAGGCCCTGCACACAAAGGGGCAGGTGCTGGGCTCAG 0975
0976 ACCTGCCAAGAGCCATATCCGGGAGGACCCTGCCCCTGACCTAAGCCCACCCCAAAGGCCAAACTCTCCACTCCC 1050
E P K S C D 1051 TCAGCTCGGACACCTTCTCCCCAGATTCCAGTAACTCCCAATCTTCTCTCTGCAGAGCCCAAATCTTGTGA 1125
1051 TCAGCTCGGACACCTTCTCCCCAGATTCCAGTAACTCCCAATCTTCTCTCTGCAGAGCCCAAATCTTGTGA 1125 K T H T C P P C P
1051 TCAGCTCGGACACCTTCTCCTCCCAGATTCCAGTAACTCCCAATCTTCTCTCTGCAGAGCCCAAATCTTGTGA 1125 K T H T C P P C P 1126 CAAAACTCACACATGCCCACCGTGCCCAGGTAAGCCAGGCCTCGCCCTCCAGCTCAAGGCGGGACAGGTG 1200 A P
1051 TCAGCTCGGACACCTTCTCCCCCAGATTCCAGTAACTCCCAATCTTCTCTCTGCAGAGCCCAAATCTTGTGA 1125 K T H T C P P C P 1126 CAAAACTCACACATGCCCACCGTGCCCAGGTAAGCCAGGCCTGGCCCTCCAGCTCAAGGCGGGACAGGTG 1200 A P 1201 CCCTAGAGTAGCCTGCATCCAGGGACAGGCCCCAGCCGGGTGCTGACACGTCCACCTCCATCTCTTCCTCAGCAC 1275 E L L G G P S V F L F P P K P K D T L M I S R T P
1051 TCAGCTCGGACACCTTCTCTCCCCAGATTCCAGTAACTCCCAATCTTCTCTCTGCAGAGCCCAAATCTTGTGA 1125 K T H T C P P C P 1126 CAAAACTCACACATGCCCACCGTGCCCAGGTAAGCCAGGCCTGGCCCTCCAGCTCAAGGCGGGACAGGTG 1200 A P 1201 CCCTAGAGTAGCCTGCATCCAGGGACAGGCCCCAGCCGGGTGGTGACACGTCCACCTCCATCTCTTCCTCAGCAC 1275 E L L G G P S V F L F P P K P K D T L M I S R T P 1276 CTGAACTCCTGGGGGGACCGTCAGTCTTCCTCTTCCCCCCAAAACCCCAAGGACACCCTCATGATCTCCCGGACCC 1350 E V T C V V V D V S H E P E V K F N W Y V D D G V
1051 TCAGCTCGGACACCTTCTCTCCCCAGATTCCAGTAACTCCCAATCTTCTCTCTC
1051 TCAGCTCGGACACCTTCTCTCCCCAGATTCCAGTAACTCCCAATCTTCTCTCTGCAGAGCCCAAATCTTGTGA 1125 K T H T C P P C P 1126 CAAAACTCACACATGCCCACCGTGCCCAGGTAAGCCAGGCCTGGCCCTCCAGCTCAAGGCGGGACAGGTG 1200 A P 1201 CCCTAGAGTAGCCTGCATCCAGGGACAGGCCCCAGCCGGGTGCTGACACGTCCACCTCCATCTCTTCCTCAGCAC 1275 E L L G G P S V F L F P P K P K D T L M I S R T P 1276 CTGAACTCCTGGGGGGGACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCC 1350 E V T C V V V D V S H E P E V K F N W Y V D D G V 1351 CTGAGGTCACATGCGTGGTGGAGCTGAGCCCAGAAGACCCTGAGGTCAACTGGTACGTGGACGGCG 1425 E V H N A K T K P R E E Q Y N S T Y R V V S V L T 1426 TGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGACGACGTACCAGGTCACCGGTGGTCTCCTCA 1500 V L H Q D W L N G K E Y K C K V S N K A L P A P I
1051 TCAGCTCGGACACCTTCTCTCCCCAGATTCCAGTAACTCCCAATCTTCTCTCTGCAGAGCCCAAATCTTGTGA 1125 K T H T C P P C P 1126 CAAAACTCACACATGCCCACCGTGCCCAGGTAAGCCAGGCCTGGCCCTCCAGCTCAAGGCGGGACAGGTG 1200 A P 1201 CCCTAGAGTAGCCTGCATCCAGGGACAGGCCCCAGCCGGGTGCTGACACGTCCACCTCCATCTCTTCCTCAGCAC 1275 E L L G G P S V F L F P P K P K D T L M I S R T P 1276 CTGAACTCCTGGGGGGACCGTCAGTCTTCCTCTTCCCCCCAAAACCCCAAGGACACCCTCATGATCTCCCGGACCC 1350 E V T C V V V D V S H E P E V K F N W Y V D D G V 1351 CTGAGGTCACATGCGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAACTGGTACGTGGACGGC 1425 E V H N A K T K P R E E Q Y N S T Y R V V S V L T 1426 TGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGACGACGACACGTACCGGTGGTCTCCTCA 1500 V L H Q D W L N G K E Y K C K V S N K A L P A P I 1501 CCGTCCTGCACCAGGACTGGCTGAATGCCAAGGAGAAGGTCCCCAACAAAGCCCTCCCAGCCCCCA 1575 E K T I S K A K
1051 TCAGCTCGGACACCTTCTCTCCCCAGATTCCAGTAACTCCCAATCTTCTCTCTGCAGAGCCCAAATCTTGTGA 1125 K T H T C P P C P 1126 CAAAACTCACACATGCCCACCGTGCCCAGGTAAGCCAGGCCTGGCCCTCCAGCTCAAGGCGGGACAGGTG 1200 A P 1201 CCCTAGAGTAGCCTGCATCCAGGGACAGGCCCCAGCCGGGTGCTGACACGTCCACCTCCATCTCTCCCCAGCAC 1275 E L L G G P S V F L F P P K P K D T L M I S R T P 1276 CTGAACTCCTGGGGGGACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCC 1350 E V T C V V V D V S H E P E V K F N W Y V D D G V 1351 CTGAGGTCACATGCGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAACTGGTACGTGGACGGC 1425 E V H N A K T K P R E E Q Y N S T Y R V V S V L T 1426 TGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGAGACACCGTACCGGTGGTCTGCGTCCTCA 1500 V L H Q D W L N G K E Y K C K V S N K A L P A P I 1501 CCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGGAGGAGAACAGGTCCCCAACAAAGCCCTCCCAGCCCCCA 1575 E K T I S K A K 1576 TCGAGGAAAACCATCTCCAAAGCCAAAGGCTGGGACCGTGGGGTGCTGGGCCCCCCA 1650 G Q P R E P Q V Y T
1051 TCAGCTCGGACACCTTCTCCCCAGATTCCAGTAACTCCCAATCTTCTCTCTGCAGAGCCCAAATCTTGTGA 1125 K T H T C P P C P 1126 CAAAACTCACACATGCCCACCGTGCCCAGGTAAGCCAGGCCCAGGCCTCCAGGCTCAAGGCGGGACAGGTG 1200 L P P C P C P C P 1201 CCCTAGAGTAGCCTGCATCCAGGGACAGGCCCCAGGCCGGGTGCAGGCCTCCAGCTCAAGGCGGGACAGGTG 1275 E L L G G P S V F L F P P K P K D T L M I S R T P 1276 CTGAACTCCTGGGGGGACCGTCAGTCTTCCTCTCTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCCGGACCC 1350 E V T C V V V D V S H E P E V K F N W Y V D D G V 1351 CTGAGGTCACATGCGTGGTGGTGGACCCGAAGACCCTGAGGTCAAGTTCAACTGGTACCTGGACGCG 1425 E V H N A K T K P R E E Q Y N S T Y R V V S V L T 1426 TGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGACAGCAGTACCAGGTACCGGGTGGTCTCCA 1500 V L H Q D W L N G K E Y K C K V S N K A L P A P I 1501 CCGTCCTGCACCAGGACTGGCTGAATGGCAAAGGTACAAGGTCCAACAAAGCCCTCCCAGCCCCCA 1575 E K T I S K A K 1576 TCGAGAAAACCATCTCCAAAGCCAAAGCTGGGACCCGTGGGGTGCACATGGACAAGGCCCGCCC
1051 TCAGCTCGACACCTTCTCTCCCCCAGATTCCAGTAACTCCCAATCTTCTCTCTGCAGAGCCCAAATCTTGTGA 1125 K T H T C P P C P 1126 CAAAACTCACACATGCCCACGTGCCCAGGTAAGCCCAGGCCTCGCCCTCCAGCTCAAGGCGGGACAGGTG 1200 A P 1201 CCCTAGAGTAGCCTGCATCCAGGGACAGGCCCCAGGCCTGGCCTCCAGCTCCAGCTCCAGCTCCAGCTCCACCTCCTCTCCTCCAGCAC 1275 E L L G G P S V F L F P P K P K D T L M I S R T P 1276 CTGAACTCCTGGGGGGACCGTCAGTCTTCCTCTCTCCCCCAAAACCCCAAGGACACCCTCATGATCTCCCGGACCC 1350 E V T C V V V D V S H E P E V K F N W Y V D D G V 1351 CTGAGGTCACATGCGTGGTGGTGGACGGCCACGAAGACCCTGAGGTCAACTGGTACCGTGACGGC 1425 E V H N A K T K P R E E Q Y N S T Y R V V S V L T 1426 TGGAGGTGCATAATGCCAAGACAAAGCCGGGGAGGACAGTACAACAGCACGTACCGGTGGTCTCCCA 1500 V L H Q D W L N G K E Y K C K V S N K A L P A P I 1501 CCGTCCTGCACCAGGACTAGCCAAAGGCCAAAGGACAAGGTCCAACAAAGCCCTCCCAGCCCCCA 1575 E K T I S K A K 1576 TCGAGAAAAACCATCTCCAAAAGCCAAAGGTGGACCGTGGGGTGCGAGGGCCACATGGACAGAGGCCGGCTCGGC 1650 C Q P R E P Q V Y T 1651 CCACCCTCTGCCCTGAGAGTGACCAAACGTTGCCAACAAAGCCCCCCGAGAACCACAGGTCTCCCAACCAA

 $Linker \leftarrow | \rightarrow FLex$ $\texttt{G} \hspace{0.1cm} \texttt{S} \hspace{0.1cm} \texttt{G} \hspace{0.1cm}$ 2026 GAGGCTCTGGTGGAGGCGGTTCAGGAGGCGGTGGATCTACCCAGGACTGCTCCTTCCAACACAGCCCCATCTCCT 2100 D F A V K I R E L S D Y L L Q D Y P V T V A S N L 2101 CCGACTTCGCTGTCAAAATCCGTGAGCTGTCTGACTACCTGCTTCAAGATTACCCAGTCACCGTGGCCTCCAACC 2175 AGSKMQGLLERVNTEIHFVTKCAFQ 2251 TCGCTGGGTCCAAGATGCAAGGCTTGCTGGAGCGCGTGAACACGCAGATACACTTTGTCACCAAATGTGCCTTTC 2325 PPPSCLRFVQTNISRLLQETSEQLV 2326 AGCCCCCCCCGGCTGTCTTCGCTCGGGAGCCACACATCTCCCGCCTCCTGCAGGAGACCTCCGAGCAGCTGG 2400 A L K P W I T R Q N F S R C L E L Q C Q P D S S T 2401 TGGCGCTGAAGCCCTGGATCACTCGCCAGAACTTCTCCCGGTGCCTGGAGCTGCAGTGTCAGCCCGACTCCTCAA 2475 L P P P W S P R P L E A T A P T A P STOP 2476 CCCTGCCACCCCATGGAGTCCCCGGCCCCTGGAGGCCCAGGCCCCGACAGCCCCGTGA

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Figure 17B

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Inventor: Jing MA

Docket No.: 549062000200 Title: PREPARATION AND APPLICATION OF ANTI-TUMOR

BIFUNCTIONAL FUSION PROTEINS

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Figure 18A

l→SP M T V L A P A W S P T T Y L L L L L L S S G L S 0001 ATGACAGTGCTGGCGCCAGCCTGGAGCCCAACAACCTATCTCCTCCTGCTGCTGCTGCTGAGCTCGGGACTCAGT 0075 G T Q D C S F Q H S P I S S D F A V K I R E L S D 0076 GGGACCCAGGACTCCTCCAACACACACCCCCATCTCCTCCGACTTCGCTGTCAAAATCCGTGAGCTGTCTGAC 0150 L L Q D Y P V T V A S N L Q D E E L C G G L W R 0151 TACCTGCTTCAAGATTACCCAGTCACCGTGGCCTCCAACCTGCAGGACGAGGAGCTCTGCGGGGGCCTCTGGCGG 0225 V L A Q R W M E R L K T V A G S K M Q G L L E R 0226 CTGGTCCTGGCACAGCGCTGGATGGAGCGGCTCAAGACTGTCGCTGGGTCCAAGATGCAAGGCTTGCTGGAGCGC 0300 NISRLLQETSEQLVALKPWITRONF 0376 AACATCTCCCGCCTCCTGCAGGAGCCTCCGAGCAGCTGGTGGCGCTGAAGCCCTGGATCACTCGCCAGAACTTC 0450 S R C L E L Q C Q P D S S T L P P P W S P R P L 0451 TCCCGGTGCCTGGAGCTGCAGTGTCAGCCCGACTCCTCAACCCTGCCACCCCCATGGAGTCCCCGGCCCCTGGAG 0525 $\label{eq:flex} FLex\leftarrow|\rightarrow hinge & hinge\leftarrow|\rightarrow CH2 \\ A T A P T A P E P K S C D K T H T C P P C P A P E \\ 0526 GCCACAGCCCCGACAGCCCCAGAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCAGCACCTGAA 0600 \\ \label{eq:flex}$ LLGGPSVFLFPPKPKDTLMISRTPE 0601 CTCCTGGGGGGACCGTCAGTCTTCCTCTCTCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAG 0675 V T C V V V D V S H E D P E V K F N W Y V D G V E 0676 GTCACATGCGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAG 0750 V H N A K T K P R E E O Y N S T Y R V V S V L T 0751 GTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGGGTCGTCGTCCTCACCGTC 0825 L H Q D W L N G K E Y K C K V S N K A L P A P I 0826 CTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAG 0900 $CH2 \leftarrow | \rightarrow CH3 \\ K~T~I~S~K~A~K~G~Q~P~R~E~P~Q~V~Y~T~L~P~P~S~R~D~E~L \\ 0901~AAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTG~0975 \\$ T K N Q V S L T C L V K G F Y P S D I A V E W E 0976 ACCAAGAACCAGGTCAGCCTGACCTGCTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGC 1050 N G Q P E N N Y K T T P P V L D S D G S F F L Y S 1051 AATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGCTCCTTCTTCCTCTACAGC 1125 K L T V D K S R W Q Q G N V F S C S V M H E A L H 1126 AAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCAC 1200 1201 AACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCCGGTAAACAGGTGCAGCTGGTGCAGTCTGGCGGTGGAGTG 1275 V Q P G R S L R L S C K A S G Y T F T S Y V M H W 1276 GTCCAGCCGGCCGCAGCCTGAGGCTGTCCTGCAAGGCATCTGGCTACACCTTCACCAGCTACGTGATGACATGG 1350 V R Q A P G K G L E W I G Y I V P Y N D G T K Y N 1351 GTGCGCCAAGCCCCCGGAAAGGGCCTCGAATGGATTGGCTACATTGTGCCTTATAATGACGGTACTAAGTACAAT 1425 E K F K G R F T I S S D K S K S T A F L O M D S L 1426 GAAAAGTTCAAGGGCAGATTTACAATATCAAGTGACAAGAGCAAGTCAACCGCATTCCTCCAAATGGACAGCTTG 1500 R P E D T A V Y Y C A R G S R Y D W Y L D Y W G Q 1501 CGTCCAGAGGACACCGCCGTATACTATTGTGTGCGCGGCAGCCGTTACGACTGGTACTTGGACTACTGGGGCCAA 1575 $VH\leftarrow|\to Linker \\ G T P V T V S S G G G G S G G G G G G S N I \\ 1576 GGCACTCCAGTCACCGTCTCCTCTGGCGGTGGAGGCCTCTGGTGGAGGCGGTTCAGGAGGCGGTGGATCTAACATC 1650$ M M T Q S P S S L S A S V G D R V T I T C K S S O 1651 ATGATGACTCAGAGCCCATCCAGCTTGAGCGCATCAGTAGGCGACCGCGTAACGATCACTTGCAAATCCTCTCAG 1725 S V L Y S S N Q K. N Y L A W Y Q Q T P G K A P K L 1726 TCAGTATTGTACTCCAGCAACCAGAAGAACTACCTGGCCGGATATCAGCAGACTCCCGGCAAAGCCCCAAAGTTG 1800

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L I Y W A S T R E S G V P S R F S G S G S G T D Y

1801 CTGATTTATTGGGCCTCCACGCGGAGTCTGGCGTGCCATCACGCTTTAGCGGCAGCGGGTCCGGTACAGATTAC 1875

T F T I S S L Q P E D I A T Y Y C H Q Y F S S Y T

1876 ACGTTTACCATTAGCAGTCTGCAGCCTGAGGACATAGCCACCTACTACTGTCACCAGTACTTTAGTTCCTACACT 1950

F G Q G T K L Q I T R SIOP

1951 TTTGGCCAGGGAACTAAACTGCAGATTACTCGATGA 1986

Docket No.: 549062000200

App No.: Not Yet Assigned

Inventor: Jing MA

Figure 18B

App No.: Not Yet Assigned Docket No.: 54
Inventor: Jing MA
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Figure 20A

	→SP SP← →VH	
0001	M E W S W I F L F L L S G T A G V H S E V CTTGCCGCCACCATGGAATGGAGTTGGATATTTCTCTTTTCTCCTGTCAGGAACTGCAGGTGCCACTCTGAGGTC (0075
0076	Q L Q Q S G P E L V K P G A S V K M S C K A S G Y CAGCTGCAGCAGCTCTGGAGCTGGGAAGCCTTGGGATAC (0150
0151	T F T S Y V M H W V K Q K P G Q G L D W I G Y I V ACATTCACTAGCTATGTTATGCACTGGGTGAAGCAGAAGCCTGGGCAGGGCCTTGACTGGATTGGATATTTGTT ($^{\circ}$	225
0226	P Y N D G T K Y N E K F K G K A T L T S D K S S CCTTACAATGATGGCACTAAGTACAATGAGAAGTTCAAAGGCAAGGCCACACTGACTTCAGACAAATCCTCCAGC (300
0301	T A Y M E L S R L T S E D S A V Y Y C V Y G S R Y ACAGCCTACATGGAGCTCAGCAGACTGACCTCTGAGGACTCTGCGGTCTATTATTGTGTCTACGGTAGTAGGTAC C .	375
0376	VH← →CH D W Y L D V W G A G T T V T V S S A S T K G P S V GACTGGTATTTAGATGTCTGGGGCGCAGGGACCACGGTCACCGTCTCCTCAGCTAGCACCAAGGGCCCATCGGTC C	450
0451	F P L A P S S K S T S G G T A A L G C L V K D Y F TTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCTGGTCAAGGACTACTTC (525
0526	P E P V T V S W N S G A L T S G V H T F P A V L Q CCCGAACCGGTGACGGTGTCTTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAG C	600
0601	S S G L Y S L S S V V T V P S S S L G T Q T Y I C TCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGC	675
0676	N V N H K P S N T K V D K K V AACGTGAATCACAAGCCCAGCAACACCAAGGTGGACAAGAAAGTTGGTGAGAGGCCAGCACAGGAGGGAG	750
0751	TCTGCTGGAAGCAGGCTCAGCGCTCCTGCCTGGACGCATCCCGGCTATGCAGCCCCAGTCCAGGCAGCAAGGCA	825
0826	GGCCCCGTCTGCCTCTTCACCCGGAGCCTCTGCCCGCCCCACTCATGCTCAGGGAGAGGGTCTTCTGGCTFTTTC 0	900
0901	CCAGGCTCTGGGCAGGCACAGGCTAGGTGCCCCTAACCCAGGCCCTGCACACAAAGGGGCAGGTGCTGGGCTCAG 0	975
0976	ACCTGCCAAGAGCCATATCCGGGAGGACCCTGCCCCTGACCTAAGCCCACCCCAAAGGCCAAACTCTCCACTCCC 1	.050
1051	E P K S C D TCAGCTCGGACACCTTCTCTCCCCAGATTCCAGTAACTCCCAATCTTCTCTCTGCAGAGCCCAAATCTTGTGA 1	105
	And the second s	125
	K T H T C P P C P CAAAACTCACACATGCCCACCGTGCCCAGGTAAGCCAGGCCAGGCCTCGCCCTCCAGCTCAAGGCGGGACAGGTG 1	
1126	K T H T C P P C P	200
1126 1201	K T H T C P P C P CAAAACTCACACATGCCCACCGTGCCCAGGTAAGCCAGGCCAGGCCTCGCCCTCCAGCTCAAGGCGGGACAGGTG 1 A P	200 275
1126 1201 1276	K T H T C P P C P CAAAACTCACACATGCCCACCGTGCCCAGGTAAGCCAGGCCCAGGCCTCCAGCTCAAGGCGGACAGGTG 1 A P CCCTAGAGTAGGCTGCATCCAGGGACAGGCCCCAGCCGGGTGCTGACACGTCCACCTCCATCTCTTCCTCAGCAC 1 E L L G G P S V F L F P P K P K D T L M I S R T P	200 275 350
1126 1201 1276 1351	CCCTAGAGTAGCCTGCATCCAGGGACAGGCCCAGGCCTGACAGGCCGGACAGGTGCAAAACTCACACATGCCCACCTGCAGCCCAGGCCGGGCCTGACACGTCAAGGCGGGACAGGTGCCACCTCAGCACCACCTCCATCTCTTCCTCAGCACCCCCCAGACCCCTCCATCTCTTCCTCAGCACCCCCCCAAAACCCCAAGGACACCCTCCATGATCTCCCCGGACCCCCCCC	200 275 350 425
1126 1201 1276 1351 1426	K T H T C P P C P CAAAACTCACACATGCCCACCGTGCCCAGGTAAGCCAGGCCAGGCCTCGCCCTCCAGCTCAAGGCGGGACAGGTG 1 A P CCCTAGAGTAGCCTGCATCCAGGGACAGGCCCCAGGCCGGGTGCTGACACGTCCACCTCCATCTCTTCCTCAGCAC 1 E L L G G P S V F L F P P K P K D T L M I S R T P CTGAACTCCTGGGGGGACCGTCAGTCTTCCTCTCTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCC 1 E V T C V V V D V S H E P E V K F N W Y V D D G V CTGAGGTCACATGCGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAACTTCAACTGGTACGTGGACGGCG 1 E V H N A K T K P R E E Q Y N S T Y R V V S V L T	200 275 350 425 500
1126 1201 1276 1351 1426 1501	CAAAACTCACACATGCCCACCGTGCCCAGGTAAGCCAGGCCTAGGCCTCAGCTCAAGGCGGGACAGGTG 1 A P CCCTAGAGTAGCCTGCATCCAGGGACAGGCCCAGGCCTGACACGCTCCAGCTCAAGGCGGGACAGGTG 1 E L L G G P S V F L F P P K P K D T L M I S R T P CTGAACTCCTGGGGGGACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCC 1 E V T C V V V D V S H E P E V K F N W Y V D D G V CTGAGGTCACATGCGTGGTGGTGGACGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCG 1 E V H N A K T K P R E E Q Y N S T Y R V V S V L T TGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGACACACAGCACGTACCGGGTGGTCTCCTCA 1 V L H Q D W L N G K E Y K C K V S N K A L P A P I	200 275 350 425 500
1126 1201 1276 1351 1426 1501 1576	K T H T C P P C P CAAAACTCACACATGCCCACGTGCCCAGGTAAGCCAGGCCTAGGCCTCAGCTCAAGGCGGACAGGTG 1 A P CCCTAGAGTAGCCTGCATCCAGGGACAGGCCCCAGCCGGGTGCTGACACGTCCACCTCCATCTCTTCCTCAGCAC 1 E L L G G P S V F L F P P K P K D T L M I S R T P CTGAACTCCTGGGGGGACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCC 1 E V T C V V V D V S H E P E V K F N W Y V D D G V CTGAAGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCG 1 E V H N A K T K P R E E Q Y N S T Y R V V S V L T TGGAGGTGCATAATGCCAAGACAAAGCCGCGGGGAGGAGCACGTACAACAGCACGTTACCGGGTGGTCTCCTCA 1 V L H Q D W L N G K E Y K C K V S N K A L P A P I CCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAACAGCACCTCCCAGCCCCCA 1 E K T I S K A K	200 275 350 425 500 575 650
1126 1201 1276 1351 1426 1501 1576 1651	CAAAACTCACACATGCCCACCTGCCCAGGTAAGCCAGGCCTAGGCCTCAGGCTCAAGGCGGACAGGTG 1 A P CCCTAGAGTAGGCTGCATCCAGGGACAGGCCCAGGCCTGACACGTCCACCTCCATCTCTTCCTCAGCAC 1 E L L G G P S V F L F P P K P K D T L M I S R T P CTGAACTCCTGGGGGGACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCC 1 E V T C V V V D V S H E P E V K F N W Y V D D G V CTGAGGTCACATGCTGTGTGGACGCCACGAAGACCCTGAGGTCAACTTCAACTGGTACGTGGACGCG 1 E V H N A K T K P R E E Q Y N S T Y R V V S V L T TGGAGGTCATAATGCCAAGACAAAGCCGCGGGAGGAGCACACAGAACACAGCACGTACCGGGTGGTCTCCTCA 1 V L H Q D W L N G K E Y K C K V S N K A L P A P I CCGTCCTGCACCAGGACTGGCTGAATGGCAAGGATACAAGTGCAAGGTCTCCAACAAAGCCCTCCCCCCCC	200 275 350 425 500 575 650 725
1126 1201 1276 1351 1426 1501 1576 1651	CAAAACTCACACATGCCCACCGTGCCCAGGTAAGCCAGGCCTAGGCCTCAGCTCAAGGCGGGACAGGTG 1 A P CCCTAGAGTAGCCTGCATCCAGGGACAGGCCCCAGGCCTGACACGTCCACCTCCATCTCTTCCTCAGCAC 1 E L L G G P S V F L F P P K P K D T L M I S R T P CTGAACTCCTGGGGGGACCGTCAGTCTTCCTCTTCCTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCC 1 E V T C V V V D V S H E P E V K F N W Y V D D G V CTGAGGTCACATGCGTGGTGGACGTCAGCCCACGAAGACCCTGAGGTCAACTGCAACTGGACGTGGACGGC 1 E V H N A K T K P R E E Q Y N S T Y R V V S V L T TGGAGGTGCATAATGCCAAGACAAAGCCGGGGGAGGAGCACACAGGACACGTACCGGGTGGTCTCCTCA 1 V L H Q D W L N G K E Y K C K V S N K A L P A P I CCGTCCTGCACCAGGACTGGCTGAATGGCAAGGATACAAGTGCAAGGTCTCCAACAAAAGCCCTCCCCAGCCCCCA 1 E K T I S K A K TCGAGAAAAACCATCTCCAAAAGCCAAAAGCTGGGACAGGGCCGGCTCGGC 1 CCACCCTCTGCCCTGAGAGTGACCAAAGCTGGGACCCTCTCCCAGCCCCCCA 1 C Q P R E P Q V Y T CCACCCTCTGCCCTGAGAGTGACCACAACCTCCTGTCCTACAGGGCCGGCTCGGC 1 CCACCCTCTGCCCTGAGAGTGACCACAACCTCTGTCCTACAGGGCCAGAACCACAGGTGTACA 1 L P P S R D E L T K N Q V S L T C L V K G F Y P S	200 275 350 425 500 575 650 725
1126 1201 1276 1351 1426 1501 1576 1651 1726 1801	CCCTAGAGTCACCACGTGCCCAGGTAAGCCAGCCCAGGCCTCGCCCTCCAGCTCAAGGCGGGACAGGTG 1 A P CCCTAGAGTAGCCTGCATCCAGGGACAGGCCCCAGCCGGGTGCTGACACGTCCACCTCCATCTCTTCCTCAGCAC 1 E L L G G P S V F L F P P K P K D T L M I S R T P CTGAACTCCTGGGGGACAGGTCTTCCTCTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCCGGACCC 1 E V T C V V V D V S H E P E V K F N W Y V D D G V CTGAGGTCACATGCGTGGTGGACGGCGGAGACCCCTCATGATCTCCCGGACCC 1 E V H N A K T K P R E E Q Y N S T Y R V V S V L T T T GGAGGTGCAAAAGCCAAGGACACACAAAGCCCAAGAACCACAAAAGCCCTCAGAGTACAACAGCACGTACCGGGTGGTCTCCAA 1 V L H Q D W L N G K E Y K C K V S N K A L P A P I CCGTCCTGCACCAAGAACCCAAGGAAGACCACAAGGCACGTACAAAGCCCTCCAAGCACAAAGCCCCCCA 1 E K T I S K A K T CGAGAAAAGCCAAAAGCCCTGAGGTGAAAAGCCCTCCCAGCCCCCA 1 C Q Q P R E P Q V Y T T CCACCCTCTGCCTCTGAGAAAAACCACCACAAAGCCCTCCCAGCCCCCA 1 C C Q P R E P Q V Y T T CCACCCTCTGCCTTGAGAAAAACCACCACAAGGTGTACAA 1 L P P S R D E L T K N Q V S L T C L V K G F Y P S CCCTGCCCCCCATCCCGGGATGACCAAGGACCACCAAGGTCAACAAAGCCCTCCCCAGCCCCCA 1 L P P S R D E L T K N Q V S L T C L V K G F Y P S CCCTGCCCCCCATCCCGGGATGACCAAGGACCACAAGGTCTCCCAACAAAGGCCTTCCCAACAAAGGCTTCTCCCAACAAAGGCCTCCCCAGCCCCCA 1 L P P S R D E L T K N Q V S L T C L V K G F Y P S CCCTGCCCCCCATCCCCGGGATGACCAAGGAACCACAAGGTCTCCCCAACAAAGGCTTCTATCCCA 1 L P P S R D E L T K N Q V S L T C L V K G F Y P S CCCTGCCCCCCATCCCGGGATGACCAAAGAACCACAAGGCTTCTATCCCA 1 L P P S R D E L T K N Q V S L T C L V K G F Y P S CCCTGCCCCCCATCCCGGGATGACCAAAGAACCAAAAGCCCTCCCCAACAAAAAACCACCAAGGTTCTATCCCA 1 L P P S R D E L T K N Q V S L T C L V K G F Y P S CCCTGCCCCCCATCCCCGGGATGACCAAAAAAAAAAACCATCTCTCTAACAAAAAAAA	200 275 350 425 500 575 650 725

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BIFUNCTIONAL FUSION PROTEINS

Inventor: Jing MA

Figure 20B

App No.: Not Yet Assigned Docket No.: 549062000200 Inventor: Jing MA
Title: PREPARATION AND APPLICATION OF ANTI-TUMOR BIFUNCTIONAL FUSION PROTEINS

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Figure 21A

→SP SP← →VH M E W S W I F L F L L S G T A G V H S E V 0001 CTTGCCGCCACCATGGAATGGAGTTGGATATTTCTCTTTCTCTGTCAGGAACTGCAGGTGTCCACTCTGAGGTC 0075
Q L Q Q S G P E L V K P G A S V K M S C K A S G Y 0076 CAGCTGCAGCAGTCTGGACCTGAGGCTTCTGGATAC 0150
T F T S Y V M H W V K Q K P G Q G L D W I G Y I V 0151 ACATTCACTAGCTATGTTATGCACTGGGTGAAGCAGAAGCCTGGGCAGGGCCTTGACTGGATTGGATATATTGTT 0225
P Y N D G T K Y N E K F K G K A T L T S D K S S S 0226 CCTTACAATGATGCACTACAATGAAGGAAGTTCAAAGGCAAGGCCACACTGACTTCAGACAAATCCTCCAGC 0300
T A Y M E L S R L T S E D S A V Y Y C V Y G S R Y 0301 ACAGCCTACATGGAGCTCAGCAGACTGACCTCTGAGGACTCTGCGGTCTATTATTGTGTCTACGGTAGTAGGTAC 0375
$\begin{array}{cccccccccccccccccccccccccccccccccccc$
F P L A P S S K S T S G G T A A L G C L V K D Y F 0451 TTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTC 0525
P E P V T V S W N S G A L T S G V H T F P A V L Q 0526 CCCGAACCGGTGACCGGTGTCTTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAG 0600
S S G L Y S L S S V V T. V P S S S L G T Q T Y I C 0601 TCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGC 0675
N V N H K P S N T K V D K K V 0676 AACGTGAATCACAAGCCCAGCAACACCCAAGGTGGACAAGAAAGTTGGTGAGAGGCCAGCACAGGGAGGG
0751 TCTGCTGGAAGCAGGCTCAGGGCTCCTGCCTGGACGCATCCCGGCTATGCAGCCCCAGTCCAGGGCAGCAAGGCA 0825
0826 GGCCCGTCTGCCTCTTCACCCGGAGCCTCTGCCCGCCCCACTCATGCTCAGGGAGAGGGTCTTCTGGCTTTTTC 0900
0901 CCAGGCTCTGGGCAGGCACAGGCTAGGTGCCCCTAACCCAGGCCCTGCACACAAAGGGGCAGGTGCTGGGCTCAG 0975
0976 ACCTGCCAAGAGCCATATCCGGGAGGACCCTGCCCCTGACCTAAGCCCACCCCAAAGGCCAAACTCTCCACTCCC 1050
E P K S C D
1051 TCAGCTCGGACACCTTCTCCCCCAGATTCCAGTAACTCCCAATCTTCTCTCTGCAGAGCCCAAATCTTGTGA 1125
1051 TCAGCTCGGACACCTTCTCCCCCAGATTCCAGTAACTCCCAATCTTCTCTCTGCAGAGCCCAAATCTTGTGA 1125 K T H T C P P C P 1126 CAAAACTCACACATGCCCACCGTGCCCAGGTAAGCCAGGCCTCGCCCTCCAGCTCAAGGCGGGACAGGTG 1200
1051 TCAGCTCGGACACCTTCTCCCCCAGATTCCAGTAACTCCCAATCTTCTCTCTGCAGAGCCCAAATCTTGTGA 1125 K T H T C P P C P
1051 TCAGCTCGGACACCTTCTCCCCCAGATTCCAGTAACTCCCAATCTTCTCTGCAGAGCCCAAATCTTGTGA 1125 K T H T C P P C P 1126 CAAAACTCACACATGCCCACCGTGCCCAGGTAAGCCAGGCCTCGCCCTCCAGCTCAAGGCGGGACAGGTG 1200 A P
1051 TCAGCTCGGACACCTTCTCCCCCAGATTCCAGTAACTCCCAATCTTCTCTCTGCAGAGCCCAAATCTTGTGA 1125 K T H T C P P C P 1126 CAAAACTCACACATGCCCACCGTGCCCAGGTAAGCCAGCC
1125 K T H T C P P C P 1126 CAAAACTCACACCTCCCCAGGTAAGCCAGGCCCAGGCCCCAGGCCCAGGCCCAAGGCGGGACAGGTG 1200
TCAGCTCGGACACCTTCTCCCCCAGATTCCAGTAACTCCCAATCTTCTCTCTGCAGAGCCCCAAATCTTGTGA 1125 K T H T C P P C P 1126 CAAAACTCACACATGCCCACGTGCCCAGGTAAGCCAGCCCAGGCCTCCAGCTCAAGGCGGGACAGGTG 1200 A P 1201 CCCTAGAGTAGCCTGCATCCAGGGACAGGCCCAGGCCGGGTGCTGACACGTCCACCTCCATCTCTTCCTCAGCAC 1275 E L L G G P S V F L F P P K P K D T L M I S R T P 1276 CTGAACTCCTGGGGGGACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCC 1350 E V T C V V V D V S H E P E V K F N W Y V D D G V 1351 CTGAGGTCACATGCGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCG 1425 E V H N A K T K P R E E Q Y N S T Y R V V S V L T
TCAGCTCGGACACCTTCTCCCCCAGATTCCAGTAACTCCCAATCTTCTCTCTGCAGAGCCCAAATCTTGTGA 1125 K T H T C P P C P 1126 CAAAACTCACACATGCCCACCGTGCCCAGGTAAGCCAGGCCCAGGCCTCCAGCTCAAGGCGGGACAGGTG 1200 A P 1201 CCCTAGAGTAGCCTGCATCCAGGGACAGGCCCCAGGCGGGTGCTGACACGTCCACCTCCATCTCTTCCTCAGCAC 1275 E L L G G P S V F L F P P K P K D T L M I S R T P 1276 CTGAACTCCTGGGGGGGACCGTCAGTCTTCCTCTCTCCCCCCAAAACCCCAAGGACACCCTCATGATCTCCCGGACCC 1350 E V T C V V V D V S H E P E V K F N W Y V D D G V 1351 CTGAGGTCACATGCGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAACTTCAACTGGTACGTGGACGGCG 1425 E V H N A K T K P R E E Q Y N S T Y R V V S V L T 1426 TGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCACGTACCAGGACCGGGTGGTCTGCGTCCTCA 1500 V L H Q D W L N G K E Y K C K V S N K A L P A P I
TCAGCTCGGACACCTTCTCCCCCAGATTCCAGTAACTCCCAATCTTCTCTCTGCAGAGCCCCAAATCTTGTGA 1125 K T H T C P P C P 1126 CAAAACTCACACATGCCCACCGTGCCCAGGTAAGCCAGGCCCAGGCCTCGCCCTCCAGCTCAAGGCGGGACAGGTG 1200 A P 1201 CCCTAGAGTAGCCTGCATCCAGGGACAGGCCCCAGGCCGGGTGCTGACACGTCCACCTCCATCTCTTCCTCAGCAC 1275 E L L G G P S V F L F P P K P K D T L M I S R T P 1276 CTGAACTCCTGGGGGGGACCGTCAGTCTTCCTCCTCCCCCCAAAACCCCAAGGACACCCTCCATGATCTCCCGGACCC 1350 E V T C V V V D V S H E P E V K F N W Y V D D G V 1351 CTGAGGTCACATGCGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGC 1425 E V H N A K T K P R E E Q Y N S T Y R V V S V L T 1426 TGGAGGTGCATAATGCCAAGACAAAGCCGGGGGAGGAGCACGACACACAC
TCAGCTCGGACACCTTCTCCCCCAGATTCCAGTAACTCCCAATCTTCTCTCGCAGAGCCCAAATCTTGTGA 1125 K T H T C P P C P 1126 CAAAACTCACACATGCCCACCGTGCCCAGGTAAGCCAGGCCCAGGCCTCGCCCTCCAGCTCAAGGCGGGACAGGTG 1200 A P 1201 CCCTAGAGTAGCCTGCATCCAGGGACAGGCCCCAGGCCGGGTGCTGACACGTCCACCTCCATCTCTTCCTCAGCAC 1275 E L L G G P S V F L F P P K P K D T L M I S R T P 1276 CTGAACTCCTGGGGGGGACCGTCAGTCTTCCTCTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGGACCC 1350 E V T C V V V D V S H E P E V K F N W Y V D D G V 1351 CTGAGGTCACATGCGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAACTTCAACTGGTACGTGGACGGCG 1425 E V H N A K T K P R E E Q Y N S T Y R V V S V L T 1426 TGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGGGTGGTCTCCTCA 1500 V L H Q D W L N G K E Y K C K V S N K A L P A P I 1501 CCGTCCTGCACCAGGACTGAATGGCAAGGATACAACGTCCAACAAAGCCCTCCCAGCCCCCA 1575 E K T I S K A K 1576 TCGAGAAAACCATCTCCAAAGCCAAAGGCCAAAGGTGGGACCGTGGGGTGCGAGGGCCACATGGACAGAGGCCGGCTCGGC 1650
TCAGCTCGGACACCTTCTCCCCCAGATTCCAGTAACTCCCAATCTTCTCTCTC
1125 TCAGCTCGGACACCTTCTCTCCTCCCAGATTCCAGTAACTCCCAATCTTCTCTCTC

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BIFUNCTIONAL FUSION PROTEINS

Inventor: Jing MA

Figure 21B

L P P P W S P R P L E A T A P T A P STOP 2476 CCCTGCCACCCCCATGGAGTCCCCGGCCCCTGGAGGCCACAGCCCCGACAGCCCCGTGA

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Inventor: Jing MA

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FUSION PROTEINS

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Figure 22A

|→SP MTV LAPAWSPTTYLLLL LLSSGLS 0001 ATGACAGTGCTGGCGCCAGCCTGGAGCCCAACAACCTATCTCCTCCTGCTGCTGCTGCTGAGCTCGGGACTCAGT 0075 G T Q D C S F Q H S P I S S D F A V K I R E L S D 0076 GGGACCCAGGACTCCTCCAACACACACCCCCATCTCCTCCGACTTCGCTGTCAAAATCCGTGAGCTGTCTGAC 0150 Y L L Q D Y P V T V A S N L Q D E E L C G G L W R 0151 TACCTGCTTCAAGATTACCCAGTCACCGTGGCCTCCAACCTGCAGGACGAGGAGCTCTGCGGGGGCCTCTGGCGG 0225 V L A Q R W M E R L K T V A G S K M Q G L L E R 0226 CTGGTCCTGGCACAGCGCTGGATGGAGCGGCTCAAGACTGTCGCTGGGTCCAAGATGCAAGGCTTGCTGGAGCGC 0300 NISRLLQETSEQLVALKPWITRQNF 0376 AACATCTCCCGCCTCCTGCAGGAGACCTCCGAGCAGCTGGTGGCGCTGAAGCCCTGGATCACTCGCCAGAACTTC 0450 S R C L E L Q C Q P D S S T L P P P W S P R P L E 0451 TCCCGGTGCCTGGAGCTGCAGTGTCAGCCCGACTCCTCAACCCTGCCACCCCCATGGAGTCCCCGGCCCCTGGAG 0525 $\label{eq:flex} FLex\leftarrow|\rightarrow hinge & hinge\leftarrow|\rightarrow CH2 \\ A T A P T A P E P K S C D K T H T C P P C P A P E \\ 0526 GCCACAGCCCCGACAGCCCCGGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCAGCACCTGAA 0600 \\ \\ \end{tabular}$ LGGPSVFLFPPKPKDTLMISRTP 0601 CTCCTGGGGGGACCGTCAGTCTTCCTCTTCCCCCCAAAACCCCAAGGACACCCTCATGATCTCCCGGACCCCTGAG 0675 V T C V V V D V S H E D P E V K F N W Y V D G V E 0676 GTCACATGCGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAG 0750 V H N A K T K P R E E O Y N S T Y R V V S V L T V 0751 GTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGGGTGGTCTGCGTCCTCACCGTC 0825 LHQDWLNGKEYKCKVSNKALPAPI 0826 CTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAG 0900 СН2←|→СН3 K T I S K A K G Q P R E P Q V Y T L P P S R D E L
0901 AAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTG 0975 T K N Q V S L T C L V K G F Y P S D I A V E W E 0976 ACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGC 1050 N G Q P E N N Y K T T P P V L D S D G S F F L Y S 1051 AATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGCTCCTTCTTCCTCTACAGC 1125 K L T V D K S R W Q Q G N V F S C S V M H E A L H 1126 AAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCAC 1200 V K P G A S V K M S C K A S G Y T F T S Y V M H W 1276 GTAAAGCCTGGGGCTTCAGTGAAGATGTCCTGCAAGGCTTCTGGATACACATTCACTAGCTATGTTATGCACTGG 1350 V K Q K P G Q G L D W I G Y I V P Y N D G T K Y N EKFKGKATLTSDKSSSTAYMELSRL 1426 GAGAAGTTCAAAGGCAAGGCCACACTGACTTCAGACAAATCCTCCAGCACAGCCTACATGGAGCTCAGCAGACTG 1500 T S E D S A V Y Y C V Y G S R Y D W Y L D V W G A 1501 ACCTCTGAGGACTCTGCGGTCTATTATTGTGTCTACGGTAGTAGGTACGACTGGTATTTAGATGTCTGGGGCGCA 1575 1576 GGGACCACGGTCACCGTCTCCTCAGGCGGTGGAGGCTCTGGTGGAGGCGGTTCAGGAGGCGGTGGATCTAACATT 1650 $Linker \leftarrow | \rightarrow V_{t}$ M M T Q S P S S L A V S A G E K V T M S C K S S O

1651 ATGATGACACAGTCGCCATCATCTCTGGCTGTGTCTGCAGGAGAAAAGGTCACTATGAGCTGTAAGTCCAGTCAA 1725

Sheet 27 of 65 S V L Y S S N Q K N Y L A W Y Q Q K P G Q S P K L 1726 AGTGTTTATACAGTTCAAATCAGAAGAACTACTTGGCCTGGTACCAGCAGAAACCAGGGCAGTCTCCTAAACTG 1800 L I Y W A S T R E S G V P D R F T G S G S G T D F 1801 CTGATCTACTGGGCATCCACTAGGGAATCTGGTGTCCCTGATCGCTTCACAGGCAGTGGATCTGGGACAGATTT 1875 T L T I S S V Q A E D L A V Y Y C H Q Y F S S Y T 1876 ACTCTTACCATCAGCAGTGTACAAGCTGAAGACCTGGCAGTTTATTACTGTCATCAATATTTCTCCTCATACACG 1950 F G G G T K L E I K R stop 1951 TTCGGAGGGGGACCAAGCTGGAAATAAAGCGGTGA

Inventor: Jing MA
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BIFUNCTIONAL FUSION PROTEINS

Figure 22B

App No.: Not Yet Assigned

Inventor: Jing MA

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FUSION PROTEINS

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Figure 23

Q Q P G A E L V K P G A S V K M S C K A S G Y T F 0076 CAGCAGCCTGGGGCTGAAGCCTGGGGCCTCAGTGAAGATGTCCTGCAAGGCTTCTGGCTACACATTT 0150

T S Y N M H W V K Q T P G R G L E W I G A I Y P G 0151 ACCAGTTACAATATGCACTGGGTAAAGCAGACACCTGGTCGGGGCCTGGAATGGATTGGAGCTATTTATCCAGGA 0225

Y M Q L S S L T S E D S A V Y Y C A R S T Y Y G G 0301 TACATGCAGCTCAGCAGCTCTGAAGACTCTGCGGTCTATTACTGTGCAAGATCGACTTACTACGGCGGT 0375

 $\begin{array}{c} V_H \leftarrow \mid \\ D \ W \ Y \ F \ N \ V \ W \ G \ A \ G \ T \ T \ V \ T \ V \ S \ A \\ 0376 \ GACTGGTACTTCAATGTCTGGGGCGCAGGGACCACGGTCACCGTCTCTGCA \\ \end{array}$

0426

Figure 24

 $| \to SP \\ M D F Q V Q I F S F L L I S A S V I M S R G Q I \\ 0001 ACCATGGATTTTCAGTGCAGATTTTCAGCTTCCTGCTAATCAGTGCTTCAGTCATAATGTCCAGAGGACAAATT 0075$

V L S Q S P A I L S A S P G E K V T M T C R A S S 0076 GTTCTCCCGGTCTCCAGCATCCTGTCTGCATCTCCAGGGGAGAGGTCACAATGACTTGCAGGGCCAGCTCA 0150

S V S Y I H W F Q Q K P G S S P K P W I Y A T S N 0151 AGTGTAAGTTACATCCACTGGTTCCAGCAGAAGCCAGGATCCTCCCCCAAACCCTGGATTTATGCCACATCCAAC 0225

L A S G V P V R F S G S G S G T S Y S L T I S R V 0226 CTGGCTTCTGGAGTCCCTGTCGCTTCAGTGGCAGTGGGTCTGGGACCTCTTACTCTCACAATCAGTAGAGTG 0300

0390

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0001	$ \!$
0076	Q Q P G A E L V K P G A S V K M S C K A S G Y T F CAGCAGCCTGGGGCTGAGCCTGGGGCCTCAGTGAAGATGTCCTGCAAGGCTTCTGGCTACACATTT 0150
0151	T S Y N M H W V K Q T P G R G L E W I G A I Y P G ACCAGTTACAATATGCACTGGGTAAAGCAGACACCTGGTCGGGGGCCTGGAATGGATTGGAGCTATTTATCCAGGA 0225
0226	N G D T S Y N Q K F K G K A T L T A D K S S S T A AATGGTGATACTTCCTACAATCAGAAGTTCAAGGGCAAGGCCACTGACTG
0301	Y M Q L S S L T S E D S A V Y Y C A R S T Y Y G G TACATGCAGCTCAGCAGCCTGACATCTGAAGACTCTGCGGTCTATTACTGTGCAAGATCGACTTACTACGGCGGT 0375
0376	$\begin{array}{cccccccccccccccccccccccccccccccccccc$
0451	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
0526	P E P V T V S W N S G A L T S G V H T F P A V L Q CCCGAACCGGTGACGGGTGTCTTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAG 0600
0601	S S G L Y S L S S V V T V P S S S L G T Q T Y I C TCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGC 0675
0676	N V N H K P S N T K V D K K V AACGTGAATCACAAGCCCAGCAACACCAAGGTGACAAGAAAGTTGGTGAGAGGCCACACAGGGAGGG
0751	TCTGCTGGAAGCAGGCTCAGCGCTCCTGCCTGGACGCATCCCGGCTATGCAGCCCCAGTCCAGGGCAGCAAGGCA 0825
0826	GGCCCCGTCTCCCCCGGAGCCTCTGCCCGCCCCACTCATGCTCAGGGAGAGGGTCTTCTGGCTTTTTC 0900
0901	CCAGGCTCTGGGCAGGCACAGGCTAGGTGCCCCTAACCCAGGCCCTGCACACAAAGGGGCAGGTGCTGGGCTCAG 0975
	ACCTGCCAAGAGCCATATCCGGGAGGACCCTGCCCCTGACCTAAGGCCAAACGCCAAACTCTCCACTCCC 1050
	E P K S C D
1051	TCAGCTCGGACACCTTCTCCCCAGATTCCAGTAACTCCCAATCTTCTCTCTGCAGAGCCCAAATCTTGTGA 1125
1126	K T H T C P P C P CAAAACTCACACATGCCCAGGTAAGCCAGCCCAGGCCTCGCCCTCCAGCTCAAGGCGGGACAGGTG 1200
1201	A P CCCTAGAGTAGCCTGCATCCAGGGACAGGCCCCAGCCGGGTGCTGACACGTCCACCTCCATCTCTTCCTCAGCAC 1275
1276	E L L G G P S V F L F P P K P K D T L M I S R T P CTGAACTCCTGGGGGGACCGTCAGTCTTCCTCTTCCCCCCAAAACCCCAAGGACACCCTCATGATCTCCCGGACCC 1350
1351	E V T C V V V D V S H E P E V K F N W Y V D D G V CTGAGGTCACATGCGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCG 1425
1426	E V H N A K T K P R E E Q Y N S T Y R V V S V L T TGGAGGTGCATAATGCCAAGACAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGGGTGGTCTGCGTCCTCA 1500
1501	V L H Q D W L N G K E Y K C K V S N K A L P A P I CCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCCAACAAAGCCCTCCCAGCCCCCA 1575
1576	E K T I S K A K TCGAGAAAACCATCTCCAAAGCCAAAGGTGGGACCCGTGGGGTGCGAGGGCCACATGGACAGAGGCCGGCTCGGC 1650
1651	G Q P R E P Q V Y T CCACCCTCTGCCCTGAGAGTGACCGCTGTACCAACCTCTGTCCTACAGGGCAGCCCCGAGAACCACAGGTGTACA 1725
1726	L P P S R D E L T K N Q V S L T C L V K G F Y P S CCCTGCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCTGGTCAAAGGCTTCTATCCCA 1800
1801	D I A V E W E S N G Q P E N N Y K T T P P V L D S GCGACATCGCCGTGGAGGAGAGACAACTACAAGACCACGCCTCCCGTGCTGGACT 1875
	D G S F F L Y S K L T V D K S R W Q Q G N V F S C CCGACGGCTCCTTCTCACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGAGACGTCTTCTCAT 1950
	S V M H E A L H N H Y T O K S L S L S P G K STOP

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0226																								R		
0226	CI	عاقات	110	166	AGT	CCC	161	TCG	CTT	CAG	1 GG	CAG	TGG	GTC	TGU	GAC	CTC	:I"I'A	CTC	rrci	CAC	:AA'I	CAC	TAG	AGTG	0300
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0301																										0375
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0376	CT	GGA	GAT	CAA	ACG	AAC	TGT	GGC	TGC	ACC	ATC	TGT	CTT	CAT	CTT	CCC	GCC	ATC	TGA	TGA	GCA	GTT	'GAA	ATC	TGGA	0450
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0451																										0525
0.51	•••			-01					0	****		CIA	100	CAO	non	.000	CAA	AGI	AC.	.010	GA.	1001	GGA	1177	CGCC	0323
	L	Q	s	G	N	s	Q	E	S	V	Т	E	Q	D	s	K	D	s	Т	Y	s	L	S	S	Т	
0526	CT	CCA	ATC	GGG	TAA	CTC	CCA	GGA	GAG	TGT	CAC	AGA	GCA	GGA	CAG	CAA	GGA	CAG	CAC	CTA	CAG	CCI	'CAC	CAG	CACC	0600
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0601																								S		
0601	CTO	JAC	JC I	÷ΑĠ	CAA	AGC.	AGA	CTA	CGA	GAA	ACA	CAA	AGT	CTA	CGC	CTG	CGA	AGT	CAC	CCA	TCA	GGG	CCT	'GAG	CTCG	0675
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Figure 27A

	$ \rightarrow SP$ $SP \leftarrow \rightarrow V_H$	
0001	M G F S R I F L F L L S V T T G V H S Q V Q L GCCACCATGGGATCAGCAGGATCTTCCTCCTCCTGTCAGTAACTACAGGTGTCCACTCCCAGGTACAACTA	0075
0076	Q Q P G A E L V K P G A S V K M S C K A S G Y T F CAGCAGCCTGGGGCTGAGCTGGAGCCTGGGGCCTCAGTGAAGATGTCCTGCAAGGCTTCTGGCTACACATTT	0150
0151	T S Y N M H W V K Q T P G R G L E W I G A I Y P G ACCAGTTACAATATGCACTGGGTAAAGCAGACACCTGGTCGGGGCCTGGAATGGATTGGAGCTATTTATCCAGGA	0225
0226	N G D T S Y N Q K F K G K A T L T A D K S S S T A AATGGTGATACTTCCTACAATCAGAAGTTCAAGGGCCAAGGCCACACTGACTG	0300
0301	Y M Q L S S L T S E D S A V Y Y C A R S T Y Y G G TACATGCAGCTCAGCAGCCTGACATCTGCAGACTCTGCGGTCTATTACTGTGCAAGATCGACTTACTACGGCGGT	0375
0376	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	0450
0451	F P L A P S S K S T S G G T A A L G C L V K D Y F TTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTC	0525
0526	P E P V T V S W N S G A L T S G V H T F P A V L Q CCCGAACCGGTGACCGGTGTCTTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAG	0600
0601	S S G L Y S L S S V V T V P S S S L G T Q T Y I C TCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGC	0675
0676	N V N H K P S N T K V D K K V AACGTGAATCACAAGCCCAGCAACACCCAAGGTGGACAAGAAAGTTGGTGAGAGGCCAGCACAGGGAGGG	0750
0751	TCTGCTGGAAGCAGGCTCAGCGCTCCTGCCTGGACGCATCCCGGCTATGCAGCCCCAGTCCAGGGCAGCAAGGCA	0825
0826	GGCCCCGTCTGCCTCTTCACCCGGAGCCTCTGCCCGCCCCACTCATGCTCAGGGAGAGGGTCTTCTGGCTTTTTC	0900
0901	CCAGGCTCTGGGCAGGCACAGGCTAGGTGCCCCTAACCCAGGCCCTGCACACAAAGGGGCAGGTGCTGGGCTCAG	0975
	ACCTGCCAAGAGCCATATCCGGGAGGACCCTGCCCCTGACCTAAGCCCACACGCCAAAGGCCAAACTCTCCACTCCC	
	EPKSCD	
1051	TCAGCTCGGACACCTTCTCCTCCCAGATTCCAGTAACTCCCAATCTTCTCTCTGCAGAGCCCCAAATCTTGTGA	1125
1126	K T H T C P P C P CAAAACTCACACAGGCCACGGGCCCAGGCCTCGCCCTCCAGGCCAAAGGCGGGACAGGTG	1200
1201	A P CCCTAGAGTAGCCTGCATCCAGGGACAGGCCCCAGCCGGGTGCTGACACGTCCACCTCCATCTCTTCCTCAGCAC	1275
1276	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	1350
1351		
	E V T C V V V D V S H E P E V K F N W Y V D D G V CTGAGGTCACATGCTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCG 1	1425
1426		
	CTGAGGTCACATGCGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCG 1 E V H N A K T K P R E E Q Y N S T Y R V V S V L T	1500
1501	CTGAGGTCACATGCGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCG E V H N A K T K P R E E Q Y N S T Y R V V S V L T TGGAGGTGCATAATGCCAAGACAAGCCGCGGGGAGGAGCAGTACAACAGCACGTACCGGGTGGTCTGCGTCCTCA V L H Q D W L N G K E Y K C K V S N K A L P A P I	1500 1575
1501 1576	CTGAGGTCACATGCGTGGTGGACGGACGACGACGACGTCAAGTTCAACTGGTACGTGGACGGCGG E V H N A K T K P R E E Q Y N S T Y R V V S V L T TGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGGGTGGTCTGCGTCCTCA 1 V L H Q D W L N G K E Y K C K V S N K A L P A P I CCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAACAAAAGCCCTCCCAGCCCCCA 1 E K T I S K A K	1500 1575 1650
1501 1576 1651	CTGAGGTCACATGCGTGGTGGACGGCGCACAGAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCG E V H N A K T K P R E E Q Y N S T Y R V V S V L T TGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGGGTGGTCTCCA 1 V L H Q D W L N G K E Y K C K V S N K A L P A P I CCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGAGTCTCCAACAAAAGCCCTCCCAGCCCCCA 1 E K T I S K A K TCGAGAAAACCATCTCCAAAGCCAAAGGTGGGACCCGTGGGGTGCGAGGGCCACATGGACAGAGGCCGGCTCGGC 1 G O P R E P O V Y T	1500 1575 1650 1725
1501 1576 1651 1726	CTGAGGTCACATGCGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCG E V H N A K T K P R E E Q Y N S T Y R V V S V L T TGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGGGTGGTCTCCA T V L H Q D W L N G K E Y K C K V S N K A L P A P I CCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGAGGTCTCCAACAAAAGCCCTCCCAGCCCCCA T E K T I S K A K TCGAGGAAAACCATCTCCAAAGCCAAAGGTGGGACCCGTGGGGTGCGAGGGCCACATGGACAGAGGCCGGCTCGGC T G Q P R E P Q V Y T CCACCCTCTGCCCTGAGAGTGACCGCTGTACCAACCTCTGTCCTACAGGGCAGCCCCCGAGAACCACAGGTGTACA T L P P S R D E L T K N Q V S L T C L V K G F Y P S	1500 1575 1650 1725

Title: PREPARATION AND APPLICATION OF ANTI-TUMOR BIFUNCTIONAL

Docket No.: 549062000200

App No.: Not Yet Assigned

Inventor: Jing MA

Figure 27B

App No.: Not Yet Assigned Docket No.: 5490 Inventor: Jing MA
Title: PREPARATION AND APPLICATION OF ANTI-TUMOR BIFUNCTIONAL FUSION PROTEINS

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Figure 28A

0001	$ \rightarrow \text{SP} \\ & \text{M G F S R I F L F L L S V T T G V H S Q V Q L} \\ & \text{GCCACCATG} \\ & \text{GATCACCAGGATCTTCCTCCTCCTGTCAGTAACTACAGGTGTCCACTCCCAGGTACAACTA} \\ \\ \cdot \rangle \\ & \text{GCCACCATG} \\ & \text{GCCACCATGC} \\ & \text{GCCACCATG} \\ & \text{GCCACCATG} \\ & \text{GCCACCATGC} \\ & GCCA$	0075
0076	Q Q P G A E L V K P G A S V K M S C K A S G Y T F CAGCAGCCTGGGGCTGAGGCTGGGGCCTCAGTGAAGATGTCCTGCAAGGCTTCTGGCTACACATTT	0150
0151	T S Y N M H W V K Q T P G R G L E W I G A I Y P G ACCAGTTACAATATGCACTGGGTAAAGCAGACACCTGGTCGGGGCCTGGAATGGATTGGAGCTATTTATCCAGGA	0225
0226	N G D T S Y N Q K F K G K A T L T A D K S S S T A AATGGTGATACTTCCTACAATCAGAAGTTCAAGGGCAAGGCCACACTGACTG	0300
0301	Y M Q L S S L T S E D S A V Y Y C A R S T Y Y G G TACATGCAGCTCAGCAGCCTGACATCTGAGACTCTGCGGTCTATTACTGTGCAAGATCGACTTACTACGGCGGT	0375
0376	$V_H \leftarrow \mid \to C_H$ D W Y F N V W G A G T T V T V S A A S T K G P S V GACTGGTACTTCAATGTCTGGGGCGCAGGGACCACGGTCACCGTCTCTGCAGCTAGCACCAAGGGCCCATCGGTC	0450
0451	F P L A P S S K S T S G G T A A L G C L V K D Y F TTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTC	0525
0526	P E P V T V S W N S G A L T S G V H T F P A V L Q CCCGAACCGGTGACGGTGTCTTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAG	0600
0601	S S G L Y S L S S V V T V P S S S L G T Q T Y I C TCCTCAGGACCTCAGCAGCGTGGCCCCCCAGCAGCTTGGGCACCCAGACCTACATCTGC	0675
0676	N V N H K P S N T K V D K K V AACGTGAATCACAAGCCCAGCAACACCAAGGTGGACAAGAAAGTTGGTGAGAGCCCAGCACAGGGAGGG	0750
0751	TCTGCTGGAAGCAGGCTCAGCGCTCCTGCCTGGACGCATCCCGGCTATGCAGCCCCAGTCCAGGCAAGGCA	0825
0826	GGCCCCGTCTGCCTCTTCACCCGGAGCCTCTGCCCGCCCCACTCATGCTCAGGGAGAGGGTCTTCTGGCTTTTTC	0900
	CCAGGCTCTGGGCAGGCACAGGCTAGGTGCCCCTAACCCAGGCCCTGCACACAAAGGGGCAGGTGCTGGGCTCAG	
	ACCTGCCAAGAGCCATATCCGGGAGGACCCTGCCCCTGACCTAAGCCCACCCCAAAGGCCAAACTCTCCACTCCC	
	E P K S C D TCAGCTCGGACACCTTCTCCCCAGATTCCAGTAACTCCCAATCTTCTCTCTGCAGAGCCCAAATCTTGTGA	
1126	K T H T C P P C P CAAAACTCACACATGCCCACGTGCCCAGGTAAGCCAGGCCTCGCCCTCCAGCTCAAGGCGGGACAGGTG	1200
1201	A P CCCTAGAGTAGCCTGCATCCAGGGACAGGCCCCAGCCGGGTGCTGACACGTCCACCTCCATCTCTTCCTCAGCAC	1275
1276	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	1350
1351	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	1425
1426	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	1500
1501	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	1575
1576	E K T I S K A K TCGAGAAAACCATCTCCAAAGCCAAAGGTGGGACCCGTGGGGTGCGAGGGCCACATGGACAGAGGCCGGCTCGGC	1650
1651	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	1725
1726	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	1800
1801	D I A V E W E S N G Q P E N N Y K T T P P V L D S GCGACATCGCCGTGGAGTGGGAGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACT	1875
1876	D G S F F L Y S K L T V D K S R W Q Q G N V F S C CCGACGGCTCCTTCTCACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCAT	1950
1951	$S \ \ V \ \ M \ \ H \ \ E \ \ A \ \ L \ \ H \ \ N \ \ H \ \ Y \ \ T \ \ Q \ \ K \ \ S \ \ L \ \ S \ \ F \ \ G \ \ K \ \ G \ \ G$ GCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCCGGTAAAGGCCGGTG	2025

Linker + FLex

G S G G G G S G G G S T Q D C S F Q H S P I S S

2026 GAGGCTCTGGTGGAGGCGGTTCAGGAGGCGGTGGATCTACCCAGGACTGCTCCTTCCAACACAGCCCCATCTCCT 2100

D F A V K I R E L S D Y L L Q D Y P V T V A S N L

2101 CCGACTTCGCTGCTGAGAAATCCGTGAGCTGTCTGACTACCTGCTTCAAGATTACCCAGTCACCGTGGCCTCCAACC 2175

Q D E E L C G G L W R L V L A Q R W M E R L K T V

2176 TGCAGGACGAGGAGGCTCTGCGGGGGCCTCTGGCGGCTGGACAGGCGGCTGAAGACTG 2250

A G S K M Q G L L E R V N T E I H F V T K C A F Q

2251 TCGCTGGGTCCAAGATGCAGGCTTGCTGGAGCGCGTGAACACGGAGATACACTTTGTCACCAAATGTGCCTTTC 2325

P P P S C L R F V Q T N I S R L L Q E T S E Q L V

2326 AGCCCCCCCCCCAGCTGTTCTTCGCTTCCAGAACAACATCTCCCGGCTCCTGCAGGAGACCTCCGAGCAGCTGG 2400

A L K P W I T R Q N F S R C L E L Q C Q P D S S T

2401 TGGCGCTGAAGCCCTGGATCACTCGCCAGAACTTCTCCCGGTGCCTGGAGGAGCTCCCCAAACCTCCCAA 2475

L P P P W S P R P L E A T A P T A P SIOP

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App No.: Not Yet Assigned

Inventor: Jing MA

FUSION PROTEINS

Figure 28B

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Inventor: Jing MA
Title: PREPARATION AND APPLICATION OF ANTI-TUMOR
BIFUNCTIONAL FUSION PROTEINS

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Figure 29A

	→SP M T V L A P A W S P T T Y L L L L L L S S G L S ATGACAGTGCTGGCGCCAGCCTGGAGCCCAACCAACCTATCTCCTCCTGCTGCTGCTGAGCTCGGGACTCAGT	0075
	P← →FLex G T Q D C S F Q H S P I S S D F A V K I R E L S D GGGACCCAGGACTGCTCCAACACACACCCCCATCTCCTCCGACTTCGCTGTCAAAATCCGTGAGCTGTCTGAC	0150
0151	Y L L Q D Y P V T V A S N L Q D E E L C G G L W R TACCTGCTTCAAGATTACCCAGTCACCGTGGCCTCCAACCTGCAGGAGGAGGTCTGCGGGGGCCTCTGGCGG	0225
0226	L V L A Q R W M E R L K T V A G S K M Q G L L E R CTGGTCCTGGCACAGCGCTGGATGGAGCGCTCAAGACTGTCGCTGGGTCCAAGATGCAAGGCTTGCTGGAGCGC	0300
0301	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	0375
0376	N I S R L L Q E T S E Q L V A L K P W I T R Q N F AACATCTCCCGCCTGCAGGAGCCTCCGAGCAGCTGGTGGCGCTGAAGCCCTGGATCACTCGCCAGAACTTC	0450
0451	S R C L E L Q C Q P D S S T L P P P W S P R P L E TCCCGGTGCCTGGAGCTGCAGCCCGACTCCTCAACCCTGCACCCCCATGGAGTCCCCGGCCCCTGGAG	0525
0526	$\begin{tabular}{lllllllllllllllllllllllllllllllllll$	0600
0601	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	0675
0676	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	0750
0751	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	0825
0826	L H Q D W L N G K E Y K C K V S N K A L P A P I E CTGCACCAGGACTGGCTGAAGGGGTACAAGGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAG	0900
0901	$CH2 \leftarrow \!$	0975
0976	T K N Q V S L T C L V K G F Y P S D I A V E W E S ACCAAGAACCAGGTCAGCCTGACCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGC	1050
	N G Q P E N N Y K T T P P V L D S D G S F F L Y S AATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCTACAGC	1125
1126	K L T V D K S R W Q Q G N V F S C S V M H E A L H AAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTCGCAC	1200
1201	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	1275
	V K P G A S V K M S C K A S G Y T F T S Y N M H W GTGAAGCCTGGGGCCTCAGTGAAGATGTCCTGCAAGGCTTCTGGCTACACATTTACCAGTTACAATATGCACTGG	1350
1351	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	1425
1426	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	1500
1501	T S E D S A V Y Y C A R S T Y Y G G D W Y F N V W ACATCTGAAGACTCTGCGGTCTATTACTGTGCAAGATCGACTTACTACGGCGGTGACTGCTACTTCAATGTCTGG	1575
1576	$V_H \leftarrow \rightarrow Linker \qquad \qquad Linker \leftarrow $ G A G T T V T V S A G G G G G G G G G G G G G G G G G G	1650
1651	$ \!$	1725

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Inventor: Jing MA

FUSION PROTEINS

Figure 29B

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CH3 CD20VH CD20VL	
СБ20VН	
	Linker
СНЗ	
CH2	
hinge	hinge
hFLex	

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Inventor: Jing MA

Title: PREPARATION AND APPLICATION OF ANTI-TUMOR BIFUNCTIONAL

FUSION PROTEINS

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Figure 31

SP←|→VH M D F Q V Q I F S F L L I S A S V I I S R G E V Q

0001 ATGGATTTTCAGGTGCAGATTTTCAGCTTCCTGCTAATCAGTGCCTCAGTCATAATATCCAGAGGAGAGGTTCAG 0075 L V E S G G G L V Q P G G S L R L S C A A S G F N 0076 CTGGTGGGTTGGCGGTGCAGCCAGCCAGCGGGGGCTCACTCCGTTTGTCCTGTGCAGCTTCTGCTTCAAC 0150 I K D T Y I H W V R Q A P G K G L E W V A R I Y P 0151 ATTAAAGACACCTATATACACTGGGTGCGTCAGGCCCCGGGTAAGGGCCTGGAATGGGTTGCAAGGATTTATCCT 0225 T N G Y T R Y A D S V K G R F T I S A D T S K N T 0226 ACGAATGGTTATACTGGATATGCCGATAGCGTCAAGGGCCGTTTCACTATAAGCGCAGACACATCCAAAAACACA 0300 A Y L Q M N S L R A E D T A V Y Y C S R W G G D G 0301 GCCTACCTGCAGATGAACAGCCTGCGTGCTGAGGACACTGCCGTCTATTATTGTTCTAGATGGGGAGGGGACGGC 0375 F Y A M D Y W G Q G T L V T V S S 0376 TTCTATGCTATGGACTACTGGGGTCAAGGAACCCTGGTCACCGTCTCCTCG

Figure 32

|→SP $\mathtt{SP} \boldsymbol\leftarrow \mid \boldsymbol\rightarrow \mathtt{V_L}$ M D F Q V Q I F S F L L I S A S V I I S R G D I Q 0001 ATGGATTTCAGGTGCAGATTTCAGCTTCCTGCTAATCAGTGCCTCAGTCATAATATCCAGAGGAGACATCCAG 0075 M T Q S P S S L S A S V G D R V T I T C R A S Q D 0076 ATGACCCAGTCCCCGAGCTCCCCTGTCCGCCTCTGTGGGCGATAGGGTTACCATCACCTGCCGTGCCAGTCAGGAT 0150 V N T A V A W Y Q Q K P G K A P K L L I Y S A S F 0151 GTGAATACTGCTGTAGCCTGGTATCAACAGAAACCAGGAAAAGCTCCGAAACTACTGATTTACTCGGCATCCTTC 0225 L Y S G V P S R F S G S R S G T D F T L T I S S L 0226 CTCTACTCTGGAGTCCCTTCTCTGGCTCCAGATCTGGGACGGATTTCACTCTGACCATCAGCAGTCTG 0300 Q P E D F A T Y Y C Q Q H Y T T P P T F G O G T K 0301 CAGCCGGAAGACTTCGCAACTTATTACTGTCAGCAACATTATACTACTCCTCCCACGTTCGGACAGGGTACCAAG 0375 $V_L \leftarrow |V_L \leftarrow |$ 0376 GTGGAGATCAAACGT

0390

0426

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Figure 33

	L van
0001	→SP SP← →VH M D F Q V Q I F S F L L I S A S V I I S R G E V Q ATGGATTTTCAGGTGCAGATTTTCAGCTTCCTGCTAATCAGTGCCTCAGTCATAATATCCAGAGGAGAGGTTCAG 0075
0076	L V E S G G G L V Q P G G S L R L S C A A S G F N CTGGTGGAGTCTGGCGTGGCAGCCAGGGGGGCTCACTCCGTTTGTCCTGTGCAGCTTCTAGC 0150
0151	I K D T Y I H W V R Q A P G K G L E W V A R I Y P ATTAAAGACACCTATATACACTGGGTGCGTCAGGCCCCGGGTAAGGGCCTGGAATGGGTTGCAAGGATTTATCCT 0225
0226	T N G Y T R Y A D S V K G R F T I S A D T S K N T ACGAATGGTTATACTAGATATGCCGATAGCGTCAAGGGCCGTTTCACTATAAGCGCAGACACATCCAAAAACACA 0300
0301	A Y L Q M N S L R A E D T A V Y Y C S R W G G D G GCCTACCTGCAGATGAACAGCCTGCTGAGGACACTGCCGTCTATTATTGTTCTAGATGGGGAGGGGACGGC 0375
0376	VH← →CH F Y A M D Y W G Q G T L V T V S S A S T K G P S V TTCTATGCTATGGACTACTGGGTCAAGGAACCCTGGTCACCGTCTCCTCGGCTAGCACCAAGGGCCCATCGGTC 0450
0451	F P L A P S S K S T S G G T A A L G C L V K D Y F TTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTC 0525
0526	P E P V T V S W N S G A L T S G V H T F P A V L Q CCCGAACCGGTGACGGGTGTCTTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAG 0600
0601	S S G L Y S L S S V V T V P S S S L G T Q T Y I C TCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGC 0675
0676	N V N H K P S N T K V D K K V AACGTGAATCACAAGCCCAGCAACACCAAGGTGGACAAGAAAGTTGGTGAGAGGCCAGCACAGGAGGGAG
0751	TCTGCTGGAAGCAGGCTCAGCGCTCCTGCCTGGACGCATCCCGGCTATGCAGCCCCAGTCCAGGGCAGCAAGGCA 0825
0826	GGCCCCGTCTGCCTCTTCACCCGGAGCCTCTGCCCGCCCCACTCATGCTCAGGGAGAGGGTCTTCTGGCTTTTTC 0900
0901	CCAGGCTCTGGGCAGGCACAGGCTAGGTGCCCCTAACCCAGGCCCTGCACACAAAGGGGCAGGTGCTGGGCTCAG 0975
0976	ACCTGCCAAGAGCCATATCCGGGAGGACCCTGCCCCTGACCTAAGCCCACCCCAAAGGCCAAACTCTCCACTCCC 1050
1051	E P K S C D TCAGCTCGGACACCTTCTCTCCCAGATTCCAGTAACTCCCAATCTTCTCTCTGCAGAGCCCCAAATCTTGTGA 1125
1126	K T H T C P P C P CAAAACTCACACAGCCCACGGGACAGGTAAGCCAGCCCAGGCCTCGCCCTCCAGCTCAAGGCGGACAGGTG 1200
1201	A P CCCTAGAGTAGCCTGCATCCAGGGACAGGCCCCAGCCGGGTGCTGACACGTCCACCTCCATCTCTCCTCAGCAC 1275
1276	E L L G G P S V F L F P P K P K D T L M I S R T P CTGAACTCCTGGGGGGACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCC 1350
1351	E V T C V V V D V S H E P E V K F N W Y V D D G V CTGAGGTCACATGCGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCG 1425
1426	E V H N A K T K P R E E Q Y N S T Y R V V S V L T TGGAGGTGCATAATGCCAAGACAAAGCCGCGGAGGAGCAGTACAACAGCACGTACCGGGTGGTCTGCGTCCTCA 1500
1501	V L H Q D W L N G K E Y K C K V S N K A L P A P I CCGTCCTGCACCAGGACTGGATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCA 1575
1576	E K T I S K A K TCGAGAAAACCATCTCCAAAGCCAAAGGTGGGACCCGTGGGGTGCGAGGGCCACATGGACAGAGGCCGGCTCGGC 1650
1651	G Q P R E P Q V Y T CCACCCTCTGCCCTGAGAGTGACCGCTGTACCAACCTCTGTCCTACAGGGCAGCCCCGAGAACCACAGGTGTACA 1725
1726	L P P S R D E L T K N Q V S L T C L V K G F Y P S CCCTGCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCTGGTCAAAGGCTTCTATCCCA 1800
1801	D I A V E W E S N G Q P E N N Y K T T P P V L D S GCGACATCGCCTGGAGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACT 1875
	D G S F F L Y S K L T V D K S R W Q Q G N V F S C CCGACGGCTCCTTCTCTCACAGCAAGCTCACAGCAAGCTCACAGCAAGCTCACAGCAAGCTCACAGCAAGCTCACAGCAAGCTCACAGCAAGCTCACAGCAAGCTCACAGCAAGCTCACAGCAAGCTCACAGCAAGCTCACAGCAAGCTCACAGCAAGCTCACAGCAAGCTCACAGCAAGCTCACAGCAAGCTCACAGCAAGCTCACAGCAAGCTCACAGCAAGAGCAAGCTCACAGCAAGAGCAAGCTCACAGCAAGAGAAAAAA

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Figure 34

	 → 5	SP																			٤	P←	→V	L		
0001	M AT	D GGA	F TTT	Q TCA	V GGT	Q GCA	I GAT	F TTT	S CAG	F CTI	L CCT	L GCT	I AAT	S CAG	A TGC	S	V AGT	I CAT	I TAA	S ATC	R CAG	G BAGG	D SAGA	I CAT	Q CCAG	0075
0076					P CCC																					0150
0151					V TGT																					0225
0226					V AGT																					0300
0301	Q CA	P GCC	E GGA	AGA	CTT	CGC.	AAC	Y TTA	Y TTA	C CTG	Q TCA	Q GCA	H ACA'	Y TTA	T FAC	T TAC	P TCC	P TCC	T CAC	F GTI	G 'CGG	Q ACA	G .GGG	T TAC	K CAAG	0375
0376				K	r R ACG	т	v																			0450
0451					V TGT(0525
0526					N TAA(0600
0601					K CAA																					0675
0676					S GAG(0711

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Figure 35A

$ \!$	0075
L V E S G G G L V Q P G G S L R L S C A A S G F N 0076 CTGGTGGAGTCTGGCTGGCTGCAGCCAGGGGGGCTCACTCCGTTTGTCCTGTGCAGCTTCTGCTTCAAC	0150
I K D T Y I H W V R Q A P G K G L E W V A R I Y P 0151 ATTAAAGACACCTATATACACTGGGTGCGTCAGGCCCCGGGTAAGGGCCTGGAATGGGTTGCAAGGATTTATCCT	0225
T N G Y T R Y A D S V K G R F T I S A D T S K N T 0226 ACGAATGGTTATACTAGATATGCCGATAGCGTCAAGGGCCGTTTCACTATAAGCGCAGACACATCCAAAAACACA	0300
A Y L Q M N S L R A E D T A V Y Y C S R W G G D G 0301 GCCTACCTGCAGATGAACAGCCTGCGTGCTGAGGACACTGCCGTCTATTATTGTTCTAGATGGGGAGGGGACGGC	0375
VH← →CH F Y A M D Y W G Q G T L V T V S S A S T K G P S V 0376 TTCTATGCTATGGACTACTGGGGTCAAGGACCCTGGTCACCGTCTCCTCGGCTAGCACCAAGGGCCCATCGGTC	0450
F P L A P S S K S T S G G T A A L G C L V K D Y F 0451 TTCCCCCTGGCACCCTCCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCTGAAGGACTACTTC	0525
P E P V T V S W N S G A L T S G V H T F P A V L Q 0526 CCCGAACCGGTGACGGTGTCTTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAG	0600
S S G L Y S L S S V V T V P S S S L G T Q T Y I C 0601 TCCTCAGGACTTACTCCCTCAGCAGCGTGGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGC	0675
N V N H K P S N T K V D K K V 0676 AACGTGAATCACAAGCCCAGCAACACCAAGGTGGACAAGAAAGTTGGTGAGAGGCCAGCACAGGAGGGAG	0750
0751 TCTGCTGGAAGCAGGCTCAGCGCTCCTGCCTGGACGCATCCCGGCTATGCAGCCCCAGTCCAGGGCAGCAAGGCA	0825
0826 GGCCCGTCTGCCTCTTCACCCGGAGCCTCTGCCCGCCCCACTCATGCTCAGGGAGAGGGTCTTCTGGCTTTTTC	0900
0901 CCAGGCTCTGGGCAGGCACAGGCTAGGTGCCCCTAACCCAGGCCCTGCACAAAGGGGCAGGTGCTGGGCTCAG	0975
0976 ACCTGCCAAGAGCCATATCCGGGAGGACCCTGCCCCTGACCTAAGCCCCACCCCAAAGGCCAAACTCTCCACTCCC	1050
E P K S C D 1051 TCAGCTCGGACACCTTCTCCCCAGATTCCAGTAACTCCCAATCTTCTCTCTGCAGAGCCCAAATCTTGTGA	1125
K T H T C P P C P 1126 CAAAACTCACACATGCCCACGTGCCCAGGTAAGCCAGGCCAGGCCTCGCCCTCCAGGTCAAGGCGGACAGGTG	1200
A P 1201 CCCTAGAGTAGCCTGCATCCAGGGACAGGCCCCAGCCGGGTGCTGACACGTCCACCTCCATCTCTTCCTCAGCAC	1275
E L L G G P S V F L F P P K P K D T L M I S R T P 1276 CTGAACTCCTGGGGGGACCGTCAGTCTTCCTCTTTCCCCCCAAAACCCCAAGGACACCCTCATGATCTCCCGGACCC	1350
E V T C V V V D V S H E P E V K F N W Y V D D G V 1351 CTGAGGTCACATGCGTGGTGGACGTGAGCCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCG	1425
E V H N A K T K P R E E Q Y N S T Y R V V S V L T 1426 TGGAGGTGCATAATGCCAAGACAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGGGTGGTCTGCGTCCTCA	1500
V L H Q D W L N G K E Y K C K V S N K A L P A P I 1501 CCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCA	1575
E K T I S K A K 1576 TCGAGAAAACCATCTCCAAAGCCAAAGGTGGGACCCGTGGGGTGCGAGGGCCACATGGACAGAGGCCGGCTCGGC	1650
G Q P R E P Q V Y T 1651 CCACCCTCTGCCCTGAGAGTGACCGCTGTACCAACCTCTGTCCTACAGGGCAGCCCCGAGAACCACAGGTGTACA	1725
L P P S R D E L T K N Q V S L T C L V K G F Y P S 1726 CCCTGCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCTGGTCAAAGGCTTCTATCCCA 1	1800
D I A V E W E S N G Q P E N N Y K T T P P V L D S 1801 GCGACATCGCCGTGGAGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACT 1	1875
D G S F F L Y S K L T V D K S R W Q Q G N V F S C 1876 CCGACGGCTCCTTCTTCTCACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCAT 1	1950

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2489

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Inventor: Jing MA

FUSION PROTEINS

Figure 35B

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Figure 36A

→SP	075
L V E S G G G L V Q P G G S L R L S C A A S G F N 0076 CTGGTGGAGTCTGGCGTGCAGCCAGGCGGGGGCTCACTCCGTTTGTCCTGTGCAGCTTCAAC 0)150
I K D T Y I H W V R Q A P G K G L E W V A R I Y P 0151 ATTAAAGACACCTATATACACTGGGTGCGTCAGGCCCCGGGTAAGGGCCTGGAATGGGTTGCAAGGATTTATCCT 02	225
T N G Y T R Y A D S V K G R F T I S A D T S K N T 0226 ACGAATGGTTATACTAGATATGCCGATAGCGTCAAGGGCCGTTTCACTATAAGCGCAGACACATCCAAAAACACA 03	300
A Y L Q M N S L R A E D T A V Y Y C S R W G G D G 0301 GCCTACCTGCAGATGAACAGCCTGCGTGAGGACACTGCCGTCTATTATTGTTCTAGATGGGGAGGGGACGGC 03	375
$ \begin{tabular}{lllllllllllllllllllllllllllllllllll$	450
F P L A P S S K S T S G G T A A L G C L V K D Y F 0451 TTCCCCCTGGCACCCTCCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGGCCTGGTCAAGGACTACTTC 05	525
PEPVTVSWNSGALTSGVHTFPAVLQ 0526 CCCGAACCGGTGACGGGTGTCTTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAG 06	600
S S G L Y S L S S V V T V P S S S L G T Q T Y I C 0601 TCCTCAGGACTCTACTCCCTCAGCAGCGTGGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGC 06	675
N V N H K P S N T K V D K K V 0676 AACGTGAATCACAAGCCCAACACCAAGGTGGACAAGAAAGTTGGTGAGAGGCCAGCACAGGGGAGGGA	750
0751 TCTGCTGGAAGCAGGCTCAGCGCTCCTGGACGCATCCCGGCTATGCAGCCCCAGTCCAGGGCAAGGCA 08	325
0826 GGCCCCGTCTGCCTCTTCACCCGGAGCCTCTGCCCGCCCCACTCATGCTCAGGGAGAGGGTCTTCTGGCTFFTTC 09	900
0901 CCAGGCTCTGGGCAGGCACAGGCTAGGTGCCCCTAACCCAGGCCCTGCACACAAAGGGGCAGGTGCTGGGCTCAG 09	975
0976 ACCTGCCAAGAGCCATATCCGGGAGGACCCTGCCCCTGACCTAAGCCCACCCCAAAGGCCAAACTCTCCACTCCC 10)50
E P K S C D 1051 TCAGCTCGGACACCTTCTCCCCAGATTCCAGTAACTCCCAATCTTCTCTCTGCAGAGCCCAAATCTTGTGA 11	L 2 5
K T H T C P P C P 1126 CAAAACTCACACATGCCCACCGTGCCCAGGTAAGCCAGGCCTGGCCCTCCAGCTCAAGGCGGGACAGGTG 12	300
A P 1201 CCCTAGAGTAGCCTGCATCCAGGGACAGGCCCCAGCCGGGTGCTGACACGTCCACCTCCATCTCTCTC	275
E L L G G P S V F L F P P K P K D T L M I S R T P 1276 CTGAACTCCTGGGGGGACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCC 13	350
E V T C V V V D V S H E P E V K F N W Y V D D G V 1351 CTGAGGTCACTGGTGGTGGTGGACGTGAGCCCACGAAGACCCTGAGGTCAACTGGTACGTGGACGGCG 14	25
E V H N A K T K P R E E Q Y N S T Y R V V S V L T 1426 TGGAGGTGCATAATGCCAAGACAAAGCCGCGGGGGGGGGG	600
V L H Q D W L N G K E Y K C K V S N K A L P A P I 1501 CCGTCCTGCACCAGGACTGGCTGAATGGCAAGGATGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCA 15	575
E K T I S K A K 1576 TCGAGAAAACCATCTCCAAAGCCAAAGGTGGGACCCGTGGGGTGCGAGGGCCACATGGACAGAGGCCGGCTCGGC 16	50
G Q P R E P Q V Y T 1651 CEACCCTCTGCCCTGAGAGTGACCGCTGTAGCAACCTCTGTCCTACAGGGCAGCCCCGAGAACCACAGGTGTACA 17:	25
L P P S R D E L T K N Q V S L T C L V K G F Y P S 1726 CCCTGCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCTGCCTG	00
D I A V E W E S N G Q P E N N Y K T T P P V L D S 1801 GCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACT 18	75
D G S F F L Y S K L T V D K S R W Q Q G N V F S C 1876 CCGACGGCTCCTTCTTCCTCTACAGCAAGCTCGCAAGAGAGCAGGTGGCAGCAGGAGGAACGTCTTCTCAT 195	50
CH← →Linker	

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Inventor: Jing MA

FUSION PROTEINS

Figure 36B

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Figure 37A

→SP M T V L A P A W S P T T Y L L L L L L S S G L S 0001 ATGACAGTGCTGGCGCCAGCCTGGAGCCCAACAACCTATCTCCTCCTGCTGCTGCTGAGCTCGGGACTCAGT 0075
SP← →FLex G T Q D C S F Q H S P I S S D F A V K I R E L S D 0076 GGGACCCAGGACTGCTCCAACACACACCCCATCTCCTCCGACTTCGCTGTCAAAATCCGTGAGCTGTCTGAC 0150
Y L L Q D Y P V T V A S N L Q D E E L C G G L W R 0151 TACCTGCTTCAAGATTACCCAGTCACCGTGGCCTCCAACCTGCAGGACGAGGAGCTCTGCGGGGGCCTCTGGCGG 0225
L V L A Q R W M E R L K T V A G S K M Q G L L E R 0226 CTGGTCCTGGCACAGCTGGATGGAGCGC 0300
V N T E I H F V T K C A F Q P P P S C L R F V Q T 0301 GTGAACACGGAGATACACTTTGTCACCAAATGTGCCTTTCAGCCCCCCCC
N I S R L L Q E T S E Q L V A L K P W I T R Q N F 0376 AACATCTCCCGCCTGCAGGAGCCTCCGAGCAGCTGCTGGCGCTGAAGCCCTGGATCACTCGCCAGAACTTC 0450
S R C L E L Q C Q P D S S T L P P P W S P R P L E 0451 TCCCGGTGCCTGGAGCTCGCGACCCCGACCCCCATGGAGTCCCCGGCCCCTGGAG 0525
FLex← →hinge hinge← →CH2 A T A P T A P E P K S C D K T H T C P P C P A P E 0526 GCCACAGCCCCGACAGCCCCGGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCAGCACCTGAA 0600
L L G G P S V F L F P P K P K D T L M I S R T P E 0601 CTCCTGGGGGGACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAG 0675
V T C V V V D V S H E D P E V K F N W Y V D G V E 0676 GTCACATGCGTGGTGGACGTGAGCCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAG 0750
V H N A K T K P R E E Q Y N S T Y R V V S V L T V 0751 GTGCATAATGCCAAGACAAGCCGCGCGGGAGGAGCAGTACAACAGCACGTACCGGGTGGTCTCGCGTCCTCACCGTC 0825
L H Q D W L N G K E Y K C K V S N K A L P A P I E 0826 CTGCACCAGGACTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAG 0900
$ \begin{array}{c} \text{CH2} \leftarrow \mid \rightarrow \text{CH3} \\ \text{K T I S K A K G Q P R E P Q V Y T L P P S R D E L} \end{array} $
0901 AAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTG 0975 T K N Q V S L T C L V K G F Y P S D I A V E W E S
0976 ACCAAGAACCAGGTCAGCCTGACCTGGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGC 1050
N G Q P E N N Y K T T P P V L D S D G S F F L Y S 1051 AATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCTACAGC 1125
K L T V D K S R W Q Q G N V F S C S V M H E A L H 1126 AAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCAC 1200
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
V Q P G G S L R L S C A A S G F N I K D T Y I H W 1276 GTGCAGCCAGGGGGCTCACTCCGTTTGTCCTGTGCAGCTTCTGCCTTCAACATTAAAGACACCTATATACACTGG 1350
V R Q A P G K G L E W V A R I Y P T N G Y T R Y A 1351 GTGCGTCAGGCCCCGGGTAAGGGCCTGGAATGGTTGCAAGGATTTATCCTACGAATGGTTATACTAGATATGCC 1425
DSVKGRFTISADTSKNTAYLQMNSL 1426 GATAGCGTCAAGGCCTTCACTATAAGCGCAGACACATCCAAAAACACAGCCTACCTGCAGATGAACAGCCTG 1500
R A E D T A V Y Y C S R W G G D G F Y A M D Y W G 1501 CGTGCTGAGGACACTGCCGTCTATTATTGTTCTAGATGGGGAGGGGACGGCTTCTATGCTATGGACTACTGGGGT 1575
VH← →Linker Q G T L V T V S S A S T K G P S V G G G G G G 1576 CAAGGAACCCTGGTCACCGTCTCCTCGGCTAGCACCAAGGGCCCATCGGTCGG

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726						_				_	•									Y GTA	-	_				K Aaa	A AGCT	1800
801	P CC	_	-	L ACI	L AC	I 'GA'	Y PPT	_		-		-	-		-	_			_	R TCG		-	_	-		S ATC	G TGGG	1875
876	_			_	T CAC	-	_					_	-				_		_	Y TTA		_	-	-		Y TTA	T TACT	1950
951	-	_		_	T	•	G TCG	-	_	T GTA	-	-		-	-		R ACG	Sto	-									1998

Figure 37B

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	CH2
hinge	·
	hFLex

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Docket No.: 549062000200 Inventor: Jing MA

Title: PREPARATION AND APPLICATION OF ANTI-TUMOR BIFUNCTIONAL **FUSION PROTEINS**

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Figure 39

 $|\rightarrow SP \\ M T V L A P A W S P T T Y L L L L L L S S G L S \\ 0001 ATGACAGTGCTGGCGCCCAGCCTGGGGCCCAACAACCTATCTCCTCCTGCTGCTGCTGGTGGTGGCTCGGGACTCAGT 0075$

T Q D C S F Q H S P I S S D F A V K I R E L S D 0076 GGGACCCAGGACTGCTCCTACAACACGCCCCATCTCCTCCGACTTCGCTGTCAAAATCCGTGAGCTGTCTGAC 0150

Y L L Q D Y P V T V A S N L Q D E E L C G G L W R 0151 TACCTGCTTCAAGATTACCCAGTCACCGTGGCCTCCAACCTGCAGGACGAGGAGCTCTGCGGGGGCCTCTGGCGG 0225

LVLAQRWMERLKTVAGSKMQGLLER 0226 CTGGTCCTGGCACAGCGCTGGATGGAGCGGCTCAAGACTGTCGCTGGGTCCAAGATGCAAGGCTTGCTGGAGCGC 0300

N I S R L L Q E T S E Q L V A L K P W I T R Q N F 0376 AACATCTCCCGCCTCCTGCAGGAGACCTCCGAGCAGCTGGTGGCGCTGAAGCCCTGGATCACTCGCCAGAACTTC 0450

S R C L E L Q C Q P D S S T L P P P W S P R P L 0451 TCCCGGTGCCTGGAGCTGCAGTGTCAGCCCGACTCCTCAACCCTGCCACCCCCATGGAGTCCCCGGCCCCTGGAG 0525

R G P Q R V A A H I T G T R G R S N T L 0601 AGAGGTCCTCAGAGAGTAGCAGCTCACATAACTGGGACCAGAGGAAGAAGCACACTTGTCTTCTCCAAACTCC 0675

L H L R N G E L V I H E K G F Y Y I Y S Q T Y F R 0751 TTGCACTTGAGGAATGGTGAACTGGTCATCCATGAAAAAGGGTTTTACTACATCTATTCCCAAACATACTTTCGA 0825

Q E E I K E N T K N D K Q M V Q Y I Y K Y T S Y

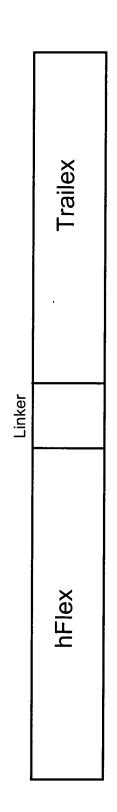
P D P I L L M K S A R N S C W S K D A E Y G L Y S 0901 CCTGACCCTATATTGTTGAAAAGTGCTAGAAATAGTTGTTGGTCTAAAGATGCAGAATATGGCTCTATTCC 0975

I Y Q G G I F E L K E N D R I F V S V T N E H L I 0976 ATCTATCAAGGGGGAATATTTGAGCTTAAGGAAAATGACAGAATTTTTGTTTCTGTAACAAATGAGCACTTGATA 1050

D M D H E A S F F G A F L V G Stop 1051 GACATGGACCATGAAGCCAGTTTTTTTGGGGGCCTTTTTAGTTGGCTAA

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Figure 41

→SP M T V L A P A W S P T T Y L L L L L L S S G L S 0001 ATGACAGTGCTGGCGCCCAGCCCTGGAGCCCAACAACCTATCTCCTCCTGCTGCTGCTGAGCTCGGGACTCAGT 0075
SP← →FLex G T Q D C S F Q H S P I S S D F A V K I R E L S D 0076 GGGACCCAGGACTGCTCCTACCACACACCACCATCTCCTCCGACTTCGCTGTCAAAAATCCGTGAGCTGTCTGAC 0150
Y L L Q D Y P V T V A S N L Q D E E L C G G L W R 0151 TACCTGCTTCAAGATTACCCAGTCACCGTGGCCTCCAACCTGCAGGACGAGGAGCTCTGCGGGGGCCTCTGGCGG 0225
L V L A Q R W M E R L K T V A G S K M Q G L L E R 0226 CTGGTCCTGGCACGCTGGATGGAGCGCCCAAGACTGCCGGGTCCAAGATGCAAGGCTTGCTGGAGCGC 0300
V N T E I H F V T K C A F Q P P P S C L R F V Q T 0301 GTGAACACGGAGATACACTTTGTCACCAAATGTGCCTTTCAGCCCCCCCC
N I S R L L Q E T S E Q L V A L K P W I T R Q N F 0376 AACATCTCCCGCCTGCAGGAGCCTCCGAGCAGCTGCTGGCGGGGCTGAAGCCCTGGATCACTCGCCAGAACTTC 0450
S R C L E L Q C Q P D S S T L P P P W S P R P L E 0451 TCCCGGTGCCTGGAGTGTCAGCCCGACTCCTCAACCCTGCCACCCCCATGGAGTCCCCGGCCCCTGGAG 0525
FLex← →Zipper A T A P T A P M K Q I E D K I E E I L S K I Y H I 0526 GCCACAGCCCCGACAGCCCCGATGAAGCAGATCGAGGACAAAATTGAGGAAATCCTGTCCAAGATTTACCACATC 0600
Zipper← →Trailex ENEIARIKKLIGETSEETISTVQEK
0601 GAGAACGAGATCGCCCGGATTAAGAAACTCATTGGCGAGACCTCTGAGGAAACCATTTCTACAGTTCAAGAAAAG 0675 Q Q N I S P L V R E R G P O R V A A H I T G T R G
0676 CAACAAAATATTTCTCCCCTAGTGAGAGAAAGAGGTCCTCAGAGAGTAGCAGCTCACATAACTGGGACCAGAGGA 0750
R S N T L S S P N S K N E K A L G R K I N S W E S 0751 AGAAGCAACACATTGTCTTCTCCAAACTCCAAGAATGAAAAGGCTCTGGGCCGCAAAATAAACTCCTGGGAATCA 0825
S R S G H S F L S N L H L R N G E L V I H E K G F 0826 TCAAGGAGTGGGCATTCATTCCTGAGCAACTTGCACTTGAGGAATGGTGAACTGGTCATCCATGAAAAAGGGTTT 0900
Y Y I Y S Q T Y F R F Q E E I K E N T K N D K Q M 0901 TACTACATCTATTCCCAAACATACTTTCGATTTCAGGAGGAAATAAAAGAAACACAAAGAACGACAAACAA
V Q Y I Y K Y T S Y P D P I L L M K S A R N S C W 0976 GTCCAATATTTACAAATACACAAGTTATCCTGACCCTATATTGTTGATGAAAAGTGCTAGAAATAGTTGTTGG 1050
S K D A E Y G L Y S I Y Q G G I F E L K E N D R I 1051 TCTAAAGATGCAGAATATGGACTCTATTCCATCTATCAAGGGGGAATATTTGAGCTTAAGGAAAATGACAGAATT 1125
F V S V T N E H L I D M D H E A S F F G A F L V G 1126 TTTGTTTCTGTAACAAATGAGCACTTGATAGACCATGAAGCCAGTTTTTTTGGGGCCTTTTTAGTTGGC 1200
STOP 1201 TAA 1203

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Inventor: Jing MA

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BIFUNCTIONAL FUSION PROTEINS

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Figure 42

l-→SP M T V L A P A W S P T T Y L L L L L L S S G L S 0001 ATGACAGTGCTGCGCCCAGCCTGGAGCCCAACAACCTATCTCCTCCTGCTGCTGCTGCTGAGCTCGGGACTCAGT 0075 G T Q D C S F Q H S P I S S D F A V K I R E L S D 0076 GGGACCCAGGACTGCTCCTACCAACACACCCCCATCTCCTCCGACTTCGCTGTCAAAATCCGTGAGCTGTCTGAC 0150 Y L L Q D Y P V T V A S N L Q D E E L C G G L W R 0151 TACCTGCTTCAAGATTACCCAGTCACCGTGGCCTCCAACCTGCAGGACGAGGAGCTCTGGGGGGGCCTCTGGCGG 0225 LVLAQRWMERLKTVAGSKMQGLLER 0226 CTGGTCCTGGCACAGCGCTGGATGGAGCGGCTCAAGACTGTCGCTGGGTCCAAGATGCAAGGCTTGCTGGAGCGC 0300 V N T E I H F V T K C A F Q P P P S C L R F V Q T 0301 GTGAACACGGAGATACACTTTGTCACCAAATGTGCCTTTCAGCCCCCCCAGCTGTCTTCGTCCAGACC 0375 NISRLLQETSEQLVALKPWITRONF 0376 AACATCTCCCGCCTCCTGCAGGAGACCTCCGAGCAGCTGGTGGCGCTGAAGCCCTGGATCACTCGCCAGAACTTC 0450 S R C L E L Q C Q P D S S T L P P P W S P R P L E 0451 TCCCGGTGCCTGGAGTGCAGCCCGAGTGCAGCCCTGGAG 0525 $\label{eq:flex} FLex\leftarrow | \rightarrow hinge \\ A \ T \ A \ P \ T \ A \ P \ E \ P \ K \ S \ C \ D \ K \ T \ H \ T \ C \ P \ P \ C \ P \ A \ P$ 0526 GCCACAGCCCCGACAGCCCCGGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCAGCACCTGAA 0600 L L G G P S V F L F P P K P K D T L M I S R T P E 0601 CTCCTGGGGGGACCGTCATCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCCGGACCCCTGAG 0675 V T C V V D V S H E D P E V K F N W Y V D G V E 0676 GTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAG 0750 V H N A K T K P R E E Q Y N S T Y R V V S V L T V 0751 GTGCATAATGCCAAGACAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGGGTGGTCTGCGTCCTCACCGTC 0825 L H Q D W L N G K E Y K C K V S N K A L P A P I E 0826 CTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAGCCCTCCCAGCCCCCATCGAG 0900 0901 AAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCATCCCGGGATGAGCTG 0975 T K N Q V S L T C L V K G F Y P S D I A V E W E S 0976 ACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGC 1050 NGQPENNYKTTPPVLDSDGSFFLYS 1051 AATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCTACAGC 1125 K L T V D K S R W Q Q G N V F S C S V M H E A 1126 AAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCAC 1200 1201 AACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCCGGTAAAGTGAGAGAAAGAGGGTCCTCAGAGAGTAGCAGCT 1275 H I T G T R G R S N T L S S P N S K N E K A L G R 1276 CACATAACTGGGACCAGAGGAAGAAGCAACACATTGTCTTCTCCAAACTCCAAGAATGAAAAGGCTCTGGGCCGC 1350 V I H E K G F Y Y I Y S Q T Y F R F Q E E I KEN 1426 GTCATCCATGAAAAAGGGTTTTACTACATCTATTCCCAAACATACTTTCGATTTCAGGAGGAAATAAAAGAAAAC 1500 T K N D K Q M V Q Y I Y K Y T S Y P D P I L L M K 1501 ACAAAGAACGACAAACAAATGGTCCAATATATTTACAAATACACAAGTTATCCTGACCCTATATTGTTGATGAAA 1575 S A R N S C W S K D A E Y G L Y S I Y Q G G I F E 1576 AGTGCTAGAAATAGTTGTTGGTCTAAAGATGCAGAATATGGACTCTATTCCATCTATCAAGGGGGAATATTTGAG 1650

L K E N D R I F V S V T N E H L I D M D H E A S F 1651 CTTAAGGAAAATGACAGAATTTTTGTTTTCTGTAACAAATGAGCACTTGATAGACCATGAAGCCAGTTTT 1725

F G A F L V G SIOP 1726 TTTGGGGCCTTTTTAGTTGGCTAA

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Trailex

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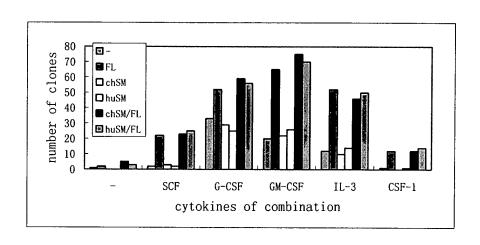
App No.: Not Yet Assigned Docket No.: 54
Inventor: Jing MA
Title: PREPARATION AND APPLICATION OF ANTI-TUMOR
BIFUNCTIONAL FUSION PROTEINS

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Figure 44



	_	SCF	G-CSF	GM-CSF	IL-3	CSF-1
-	1	2	33	20	12	1
FL	2	22	52	65	52	12
chSM	0	3	29	22	10	0
huSM	0	2	25	26	14	1
chSM/FL	5	23	59	75	46	12
huSM/FL	3	25	56	70	50	14

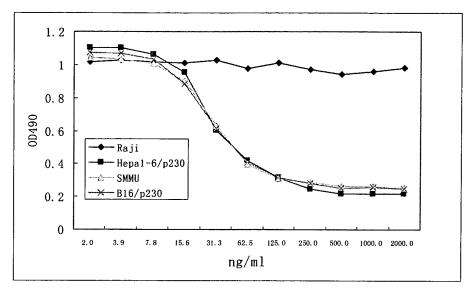


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(×10 ₆)	huSM/FL	2.8	8.5	55	133	182	591	191	601	3.5	4.3	5.9	3.7	16.9	10.1	5.1	7.0	2.0	6.1	11.5	33	36	31	15	13
CD11c ⁺ (DC)	chSM/FL	3.0	8.0	56	136	189	191	156	114	3.0	4.5	5.6	3.9	17.3	8.6	4.8	6.7	8.1	2.0	11.7	32	35	29	91	14
CI	FL	3.0	5.0	35	85	180	190	180	150	2.0	3.0	5.0	5.5	18.5	9.0	2.5	8.0	2.0	3.0	15.0	20	39	29	61	14
(×10 ₆)	huSM/FL	6.5	10.0	18.5	30	31	47	. 35	51	4.8	7.0	4.8	9.5	3.0	20	7.5	2.3	1.2	1.1	1.3	2.1	2.0	6.1	4.5	3.4
CD3 ⁺ NK1.1 ⁺ (NK)	chSM/FL	6.0	9.0	18.0	28	32	49	33	49	4.5	6.9	4.5	6.6	2.8	61	8.0	2.0	1.0	1.2	1.2	1.9	1.9	5.7	4.2	3.7
CD3 ⁺]	FL	7.0	5.0	=	21	17	50	27	41	5.0	0.9	5.0	9.0	3.0	61	0.6	2.0	1.0	1.8	1.8	2.5	2.0	5.0	5.0	4.0
(×10 ₆)	huSM/FL	40	53	82	70	83	55	40	28	1.1	2.0	1.9	2.1	3.8	5.2	3.0	3.5	2.5	5.3	1.8	1.8	2.1	1.6	3.5	2.0
CD3 ⁺ NK1.1'(T)	chSM/FL	38	55	81	72	80	53	39	26	1.3	1.8	1.8	1.9	3.5	5.5	2.8	3.4	2.0	5.5	1.8	1.5	1.9	1.5	3.4	1.8
CD3	FL	40	50	76	89	75	50	38	22	1.0	1.5	1.5	1.5	3.8	5.6	3.0	3.0	2.0	5.9	1.9	1.5	2.5	2.5	3.9	1.9
(×10°)	huSM/FL	3.5	4.0	5.5	14	23	30	17	01	6.0	3.5	4.5	11.0	19.0	16.0	6.5	3.0	1.5	2.0	2.0	5.0	4.5	5.5	4.5	3.5
CD3 NK1.1 ⁺ (NK) (×1	chSM/FL	3.0	4.0	5.0	15	21	29	18	12	1.0	3.0	5.0	12.0	18.0	17.0	6.0	3.0	1.0	2.0	1.8	4.5	5.0	5.2	4.0	3.3
CD3.	FL	2.0	3.0	6.0	16	17	24	20	6	1.0	2.0	3.0	13.0	20	=	5.0	2.0	2.0	1.0	1.5	4.0	4.0	4.0	4.0	3.0
	ţį,	0	3	9	∞	2	12	15	-81	0	3	9	∞	9	12	15	18	0	3	9	∞	10	12	15	-81
Item	Treatment	*			noolus					1.	<u>.</u>		liver	<u> </u>							Bone	marrow			

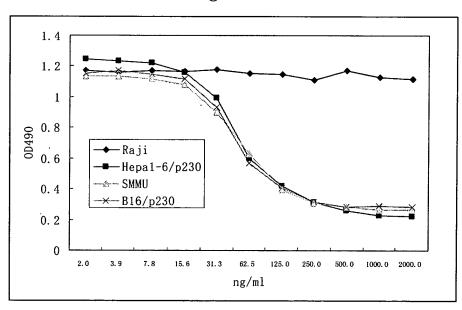
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Figure 46A



chSM5-1

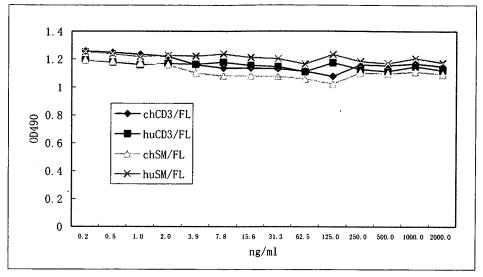
Figure 46B



huSM5-1

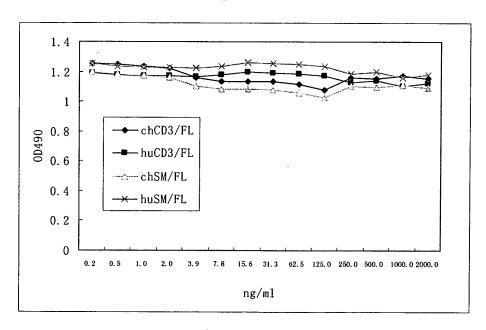
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Figure 47A



B16

Figure 47B

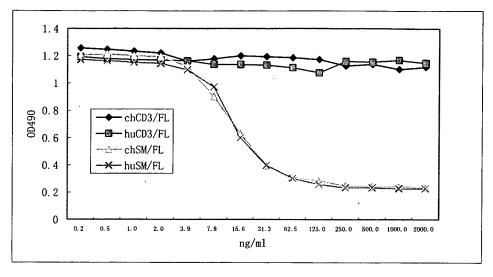


hepa1-6

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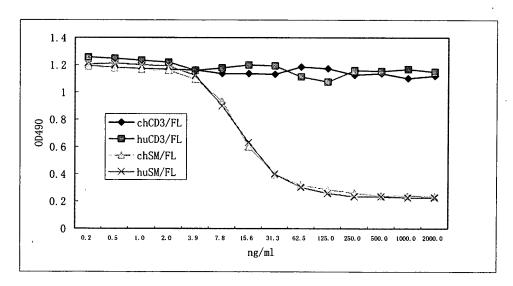
Docket No.: 549062000200

Figure 47C



B16/p230

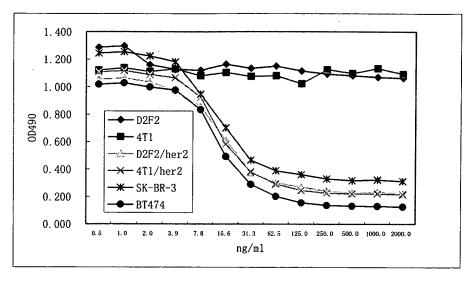
Figure 47D



hepa1-6/p230

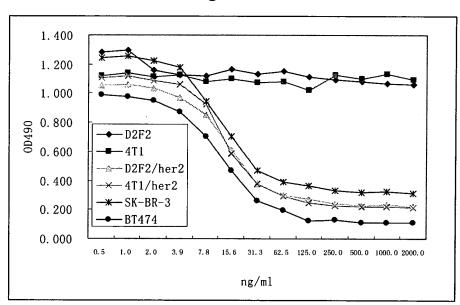
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Figure 48A



FL/her2

Figure 48B

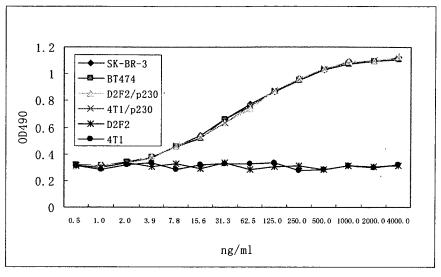


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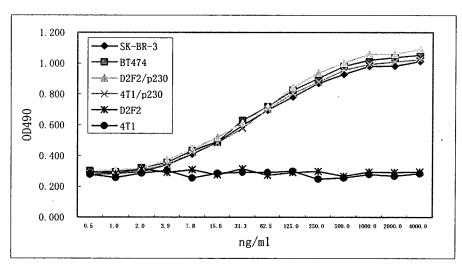
Docket No.: 549062000200

Figure 49A



her2/FL

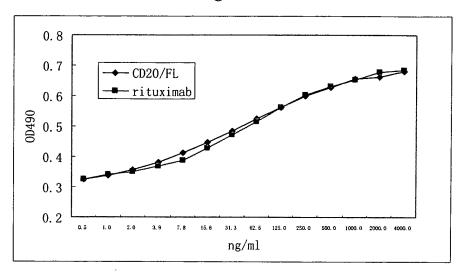
Figure 49B



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Figure 50



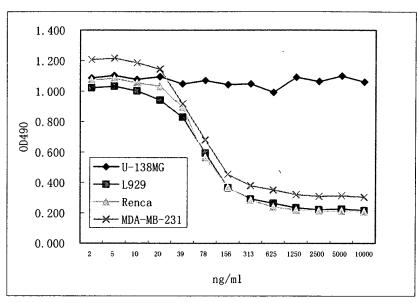
Docket No.: 549062000200 App No.: Not Yet Assigned

Inventor: Jing MA
Title: PREPARATION AND APPLICATION OF ANTI-TUMOR

BIFUNCTIONAL FUSION PROTEINS

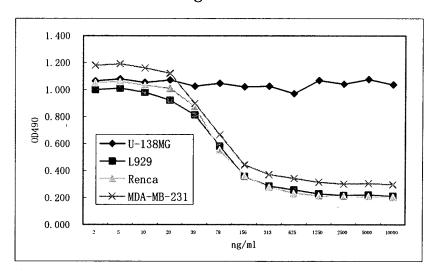
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Figure 51A



Trail/FL

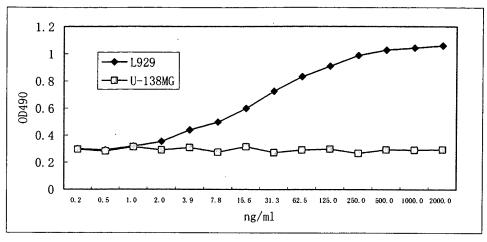
Figure 51B



Trail

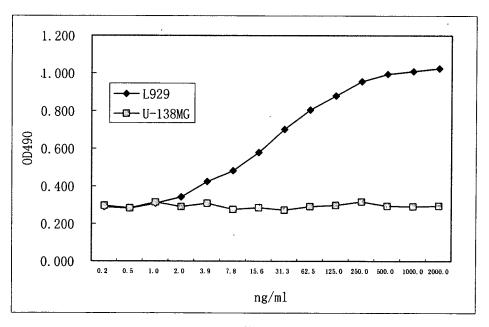
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Figure 52A



Trail/FL

Figure 52B



Trail

App No.: Not Yet Assigned Inventor: Jing MA

Title: PREPARATION AND APPLICATION OF ANTI-TUMOR BIFUNCTIONAL FUSION PROTEINS

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Figure 53

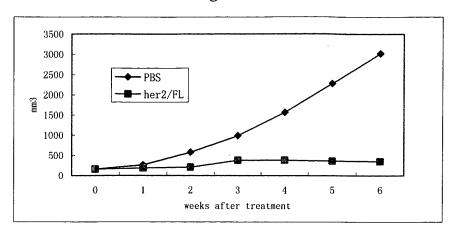


Figure 54

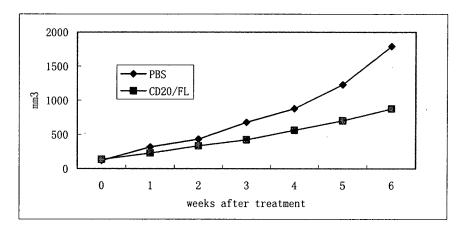
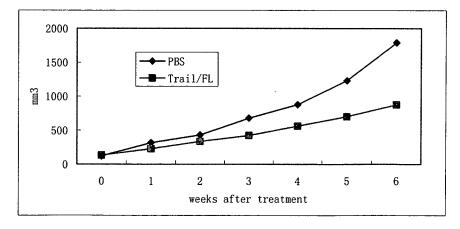


Figure 55



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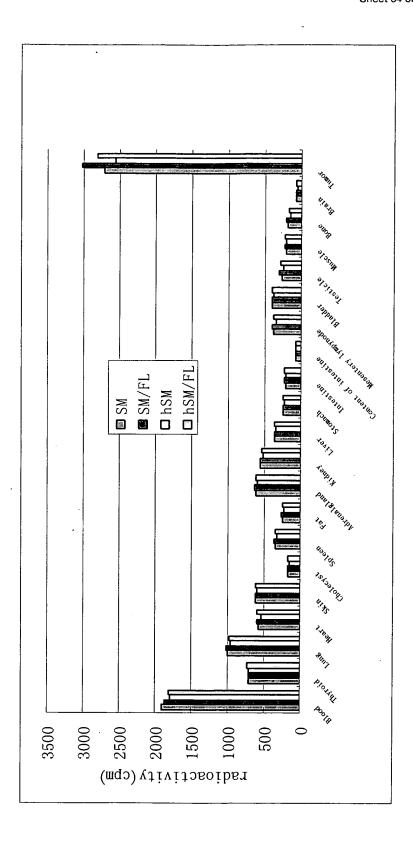


FIGURE 56

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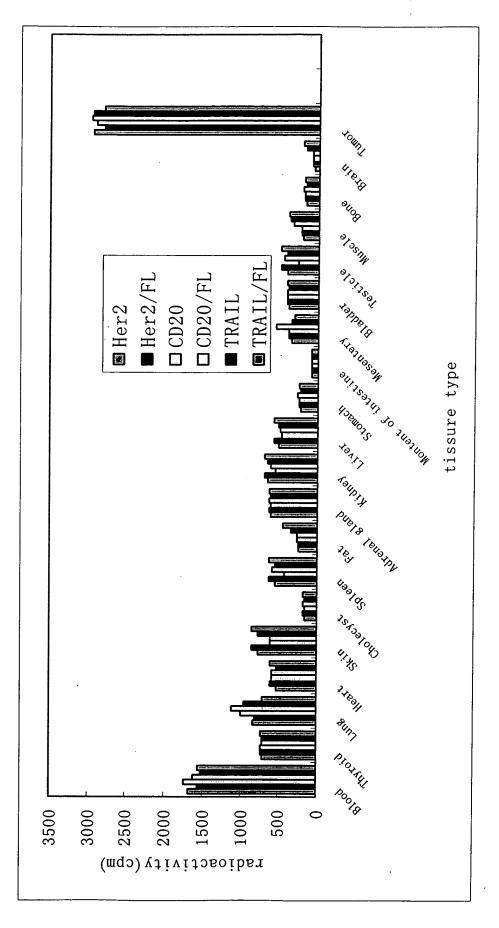


FIGURE 57